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TITLE: Infertility due to antisperm antibodies.

AUTHORS: Ohl DA; Naz RK

AUTHOR AFFILIATION: Department of Surgery, University of Michigan Medical Center, Ann Arbor 48109, USA.

SOURCE: Urology 1995 Oct;46(4):591-602

CITATION IDS: PMID: 7571238 UI: 96008686

ABSTRACT: Immunoinfertility is an important problem, involving a significant number of infertile couples. Although the presence of antibodies on sperm has better prognostic value than those in serum or seminal plasma, it may not be the sole authentic evidence of immunoinfertility. Infertility from antisperm antibodies is likely only when they bind to a relevant sperm antigen involved in a specific fertility function. The variance in functional deficits seen in immunologic infertility is most likely related to antibodies directed at different sperm antigens or different class, subclass, or isotypes. Antibodies to FA-1 seem to be of significant importance in human immunoinfertility. In approaching couples with infertility, a high index of suspicion for antibodies is necessary to avoid misdiagnosis. In the optimal situation, all semen analyses should be screened for sperm-bound antibodies, but if this is impractical, testing should be performed on high-risk individuals (Table I). In couples in which the man has sperm-bound antibodies, and in whom there is no identifiable female factor, treatment should be instituted. Most treatments for immunoinfertility have been disappointing because of poor results, adverse effects, or high cost. Corticosteroid therapy has shown some promise in published reports (mostly poorly designed studies), but increase in pregnancy rate is modest and adverse effects may be significant. In our opinion, informed consent should be documented prior to institution of corticosteroid therapy, and subjects should be closely monitored. Advanced reproductive technologies offer a higher safety profile, and, with increasing technology, higher pregnancy rates. We recommend progressing from "low-tech" procedures, such as IUI and reserving the higher level procedures, such as IVF and ICSI, for those couples in whom

pregnancy does not occur. The highest level reproductive technologies give the best current prospects for pregnancy in patients with this difficult problem but also are invasive and costly. It is hoped that further work in the laboratory will give rise to newer, safer, and less expensive effective treatments in the very near future.

MAIN MESH HEADINGS:	Autoantibodies/*immunology Infertility, Male/*immunology Spermatozoa/*immunology
ADDITIONAL MESH HEADINGS:	Antigens, Surface/immunology Female Human Infertility, Male/therapy Male Risk Factors 1995/10 1995/01 00:00
PUBLICATION TYPES:	JOURNAL ARTICLE REVIEW REVIEW, TUTORIAL
CAS REGISTRY NUMBERS:	0 (Antigens, Surface) 0 (Autoantibodies)
LANGUAGES:	Eng

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                   Substances (PICCS) has been added to CHEMLIST
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=> s female infertility treatment

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=> s female infertility treatment

L1          12 FEMALE INFERTILITY TREATMENT

=> d l1 all 1-12
```

L1 ANSWER 1 OF 12 MEDLINE
AN 97365075 MEDLINE
DN 97365075
TI **Female infertility**: **treatment** options for complicated cases. The ESHRE Capri Workshop. European Society for Human Reproduction and Embryology.
AU Anonymous
SO HUMAN REPRODUCTION, (1997 Jun) 12 (6) 1191-6.
Journal code: HRP. ISSN: 0268-1161.
CY ENGLAND: United Kingdom
DT Conference; Conference Article; (CONGRESSES)
LA English
FS Priority Journals
EM 199711
CT Check Tags: Female; Human
Abortion, Habitual: ET, etiology
Abortion, Habitual: TH, therapy
Adult
Age Factors
Anovulation: PP, physiopathology
Anovulation: TH, therapy
Body Weight
Endometriosis: CO, complications
Fallopian Tube Diseases: SU, surgery
Gonadorelin: SE, secretion
Infertility, Female: PA, pathology
Infertility, Female: PP, physiopathology
*Infertility, Female: TH, therapy
Oocyte Donation
Ovulation Induction
Pregnancy
Reproduction Techniques
RN 33515-09-2 (Gonadorelin)

L1 ANSWER 2 OF 12 MEDLINE
AN 94072524 MEDLINE
DN 94072524
TI Infertility treatment: from cookery to science. The epidemiology of randomised controlled trials.
AU Vandekerckhove P; O'Donovan P A; Lilford R J; Harada T W
CS Institute of Epidemiology and Health Services Research, University of Leeds, UK..
SO BRITISH JOURNAL OF OBSTETRICS AND GYNAECOLOGY, (1993 Nov) 100 (11) 1005-36. Ref: 324
Journal code: AZC. ISSN: 0306-5456.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199403
AB OBJECTIVES: To review the epidemiology of published randomised controlled trials in infertility treatment over the last 25 years, with special emphasis on the number and quality of trials. DESIGN: Computer literature review by MEDLINE backed up by a manual search of 41 journals. Each trial was classified according to the methodology described and quality criteria. The results were recorded in a computer database. Odds ratios (OR) and confidence intervals (CI) were calculated where the data were sufficient. SUBJECTS: Couples suffering from primary or secondary infertility. The trials studied 33,761 patients overall. SETTING: Institute of Epidemiology and Health Services Research, Leeds. RESULTS: Five hundred and one randomised trials in male and **female infertility treatment** were identified between 1966 and 1990. Pregnancy was an outcome in 291 (58%) and these were the subject of detailed analysis. Two hundred and twenty-four (77%) and 67 (23%) 'pregnancy trials' were concerned, respectively, with female and male infertility. Four per cent of the trials were preceded by a sample size calculation, and the average sample size was 96 patients (range 5-933); 700 patients per group would be required to demonstrate plausible success rates for most treatments. The method of randomisation was unstated or pseudo-randomised in 206 (71%) of trials where pregnancy was an outcome. Only 29 (5.8%) of studies were multicentre. The method of confirmation of pregnancy was omitted for 70% of papers. Cross-over design was used in 103 (21%) of cases. Meta-analysis is possible for selected topics such as the use of anti-oestrogens in idiopathic oligospermia and unexplained female infertility. Eight cases of double reporting were identified.
CONCLUSIONS: Trials using randomised methodology were relatively few in comparison with other branches of medicine, although their use is important in the evaluation of treatment for infertility as treatment-independent pregnancy is common. It was encouraging to note that an exponential increase in the use of this methodology occurred during the last three years, especially in association with assisted conception techniques, and meta-analysis has become possible for selected topics. However, many trials suffer from an unrealistically small sample size, inappropriate use of cross-over design or pseudo-randomisation. The trend towards properly controlled studies should be encouraged but these studies should be of improved quality and organised on a multicentre or even international basis.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
*Infertility: TH, therapy
Pregnancy
*Randomized Controlled Trials: SN, statistics & numerical data
Randomized Controlled Trials: ST, standards
Treatment Outcome

L1 ANSWER 3 OF 12 MEDLINE
AN 81247201 MEDLINE
DN 81247201
TI [Microsurgery in **female infertility treatment** (author's transl)].
Mikrochirurgische Behandlung der weiblichen Sterilitat.
AU Floersheim Y
SO SCHWEIZERISCHE RUNDSCHAU FUR MEDIZIN PRAXIS, (1980 Dec 2) 69 (48) 1780-5.
Journal code: SRM. ISSN: 0369-8394.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA German
EM 198111
CT Check Tags: Female; Human
English Abstract
*Fallopian Tubes: SU, surgery
*Infertility, Female: SU, surgery
Microsurgery: MT, methods
Pregnancy

L1 ANSWER 4 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 97194431 EMBASE
DN 1997194431
TI **Female infertility**: **Treatment** options for complicated cases.
AU Diedrich K.; Collins J.; Baird D.T.; Evers J.L.H.; Crosignani P.G.; Tarlatzis B.; Cooke I.; Glasier A.; Devroey P.; Van Steirteghem A.; Benagiano G.; Cohen J.; Diczfalusy E.; Ragni G.
SO Human Reproduction, (1997) 12/6 (1191-1196).
Refs: 76
ISSN: 0268-1161 CODEN: HUREEE
CY United Kingdom
DT Journal; General Review
FS 010 Obstetrics and Gynecology
LA English
CT Medical Descriptors:
*female infertility: TH, therapy
adult
anovulation: TH, therapy
endometriosis: TH, therapy
female
fertility
human
lean body weight
male
maternal age
medical decision making
obesity
oocyte donation
ovulation induction
patient selection
review
spontaneous abortion: TH, therapy
uterine tube occlusion: SU, surgery
workshop

L1 ANSWER 5 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 93344188 EMBASE
DN 1993344188
TI Infertility treatment: From cookery to science. The epidemiology of randomised controlled trials.
AU Vandekerckhove P.; O'Donovan P.A.; Lilford R.J.; Harada T.W.
CS University of Leeds, Department of Clinical medicine, Inst. Epidemiology/Hlth. Serv. Res., 34 Hyde Terrace,Leeds LS2 9LN, Japan
SO British Journal of Obstetrics and Gynaecology, (1993) 100/11 (1005-1036). ISSN: 0306-5456 CODEN: BJOGAS
CY United Kingdom
DT Journal; Article
FS 003 Endocrinology
010 Obstetrics and Gynecology
037 Drug Literature Index
LA English
SL English
AB Objectives: To review the epidemiology of published randomised controlled trials in infertility treatment over the last 25 years, with special emphasis on the number and quality of trials. Design: Computer literature review by MEDLINE backed up by a manual search of 41 journals. Each trial was classified according to the methodology described and quality criteria. The results were recorded in a computer database. Odds ratios (OR) and confidence intervals (CI) were calculated where the data were sufficient. Subjects: Couples suffering from primary or secondary infertility. The trials studied 33761 patients overall. Setting: Institute of Epidemiology and Health Services Research, Leeds. Results: Five hundred and one randomised trials in male and **female infertility treatment** were identified between 1966 and 1990. Pregnancy was an outcome in 291 (58%) and these were the subject of detailed analysis. Two hundred and twenty-four (77%) and 67 (23%) 'pregnancy trials' were concerned, respectively, with female and male infertility. Four per cent of the trials were preceded by a sample size calculation, and the average sample size was 96 patients (range 5-933); 700 patients per group would be required to demonstrate plausible success rates for most treatments. The method of randomisation was unstated or pseudo-randomised in 206 (71%) of trials where pregnancy was an outcome. Only 29 (5.8%) of studies were multicentre. The method of confirmation of pregnancy was omitted for 70% of papers. Cross-over design was used in 103 (21%) of cases. Meta-analysis is possible for selected topics such as the use of anti-oestrogens in idiopathic oligospermia and unexplained female infertility. Eight cases of double reporting were identified. Conclusions: Trials using randomised methodology were relatively few in comparison with other branches of medicine, although their use is important in the evaluation of treatment for infertility as treatment-independent pregnancy is common. It was encouraging to note that an exponential increase in the use of this methodology occurred during the last three years, especially in association with assisted conception techniques, and meta-analysis has become possible for selected topics. However, many trials suffer from an unrealistically small sample size, inappropriate use of cross-over design or pseudo-randomisation. The trend towards properly controlled studies should be encouraged but these studies should be of improved quality and organised on a multicentre or even international basis.

CT Medical Descriptors:
*infertility: TH, therapy
*infertility: DT, drug therapy
article
artificial insemination
clinical trial
female
fetus outcome
human
male
priority journal
Drug Descriptors:
*antiestrogen: CT, clinical trial
*antiestrogen: DT, drug therapy
*ascorbic acid: CT, clinical trial
*ascorbic acid: DT, drug therapy
*buserelin: DT, drug therapy
*buserelin: CT, clinical trial
*clomifene: CT, clinical trial
*clomifene: DT, drug therapy
*corticosteroid: CT, clinical trial
*corticosteroid: DT, drug therapy
*follitropin: CT, clinical trial
*follitropin: DT, drug therapy
*gonadorelin agonist: DT, drug therapy
*gonadorelin agonist: CT, clinical trial
*hormone: DT, drug therapy
*hormone: CT, clinical trial
*leuprorelin: DT, drug therapy
*leuprorelin: CT, clinical trial
*nafarelin: CT, clinical trial
*nafarelin: DT, drug therapy
bromocriptine: DT, drug therapy
bromocriptine: CT, clinical trial
chorionic gonadotropin: DT, drug therapy
chorionic gonadotropin: CT, clinical trial
cyclofenil: CT, clinical trial
cyclofenil: DT, drug therapy
danazol: DT, drug therapy
danazol: CT, clinical trial
dexamethasone: DT, drug therapy
dexamethasone: CT, clinical trial
dydrogesterone: DT, drug therapy
dydrogesterone: CT, clinical trial
gestrinone: DT, drug therapy
gestrinone: CT, clinical trial
growth hormone: DT, drug therapy
growth hormone: CT, clinical trial
human menopausal gonadotropin: CT, clinical trial
human menopausal gonadotropin: DT, drug therapy
levamisole: CT, clinical trial
levamisole: DT, drug therapy
medroxyprogesterone acètate: DT, drug therapy
medroxyprogesterone acetate: CT, clinical trial
mesterolone: CT, clinical trial
mesterolone: DT, drug therapy
methylprednisolone: DT, drug therapy
methylprednisolone: CT, clinical trial

progesterone: CT, clinical trial
progesterone: DT, drug therapy
tamoxifen: CT, clinical trial
tamoxifen: DT, drug therapy
unindexed drug

RN (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (buserelin) 57982-77-1; (clomifene) 911-45-5; (follitropin) 9002-68-0; (leuprorelin) 53714-56-0, 74381-53-6; (nafarelin) 76932-56-4; (bromocriptine) 25614-03-3; (chorionic gonadotropin) 9002-61-3; (cyclofenil) 2624-43-3; (danazol) 17230-88-5; (dexamethasone) 50-02-2; (dydrogesterone) 152-62-5; (gestrinone) 16320-04-0; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (human menopausal gonadotropin) 61489-71-2; (levamisole) 14769-73-4, 16595-80-5; (medroxyprogesterone acetate) 71-58-9; (mesterolone) 1424-00-6; (methylprednisolone) 6923-42-8, 83-43-2; (progesterone) 57-83-0; (tamoxifen) 10540-29-1

L1 ANSWER 6 OF 12 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:399960 BIOSIS
DN PREV199799699163
TI **Female infertility**: **Treatment** options for complicated cases. Capri, Italy, August 22-23, 1996.
AU Eshre Capri Workshop
SO Human Reproduction (Oxford), (1997) Vol. 12, No. 6, pp. 1191-1196. ISSN: 0268-1161.
DT Conference; Report
LA English
CC Reproductive System - General; Methods *16501
Gerontology *24500
IT Major Concepts
Aging; Reproductive System (Reproduction)
IT Miscellaneous Descriptors
AGE; ANOVULATION; ART; ASSISTED REPRODUCTION METHOD; ASSISTED REPRODUCTIVE TECHNIQUE; BODY WEIGHT; EARLY PREGNANCY LOSS; ENDOCRINE DISEASE/GONADS; ENDOMETRIOSIS; FECUNDABILITY; FEMALE INFERTILITY; OOCYTE DONATION; OVARIAN STIMULATION; REPRODUCTIVE SYSTEM; REPRODUCTIVE
SYSTEM DISEASE/FEMALE; SURGERY; TUBAL DAMAGE

L1 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:69031 BIOSIS
DN PREV199497082031
TI Infertility treatment: From cookery to science: The epidemiology of randomised controlled trials.
AU Vandekerckhove, P.; O'Donovan, P. A.; Lilford, R. J.; Harada, T. W.
CS Univ. Leeds, Dep. Clinical Med., Inst. Epidemiology Health Serv. Res., 34 Hyde Terrace, Leeds LS2 0LN UK
SO British Journal of Obstetrics and Gynaecology, (1993) Vol. 100, No. 11, pp. 1005-1036.
ISSN: 0306-5456.
DT Article
LA English
AB Objectives - To review the epidemiology of published randomized controlled trials in infertility treatment over the last 25 years, with special emphasis on the number and quality of trials. Design - Computer literature review by MEDLINE backed up by a manual search of 41 journals. Each trial was classified according to the methodology described and quality criteria. The results were recorded in a computer database. Odds ratios (OR) and confidence intervals (CI) were calculated where the data were sufficient. Subjects - Couples suffering from primary or secondary infertility. The trials studied 33 761 patients overall. Setting - Institute of Epidemiology and Health Services Research, Leeds. Results - Five hundred and one randomized trials in male and **female infertility treatment** were identified between 1966 and 1990. Pregnancy was an outcome in 291 (58%) and these were the subject of detailed analysis. Two hundred and twenty-four (77%) and 67 (23%) 'pregnancy trials' were concerned, respectively, with female and male infertility. Four per cent of the trials were preceded by a sample size calculation, and the average sample size was 96 patients (range 5-933); 700 patients per group would be required to demonstrate plausible success rates for most treatments. The method of randomization was unstated or pseudo-randomized in 206 (71%) of trials where pregnancy was an outcome. Only 29 (5.8%) of studies were multicenter. The method of confirmation of pregnancy was omitted for 70% of papers. Cross-over design was used in 103 (21%) of cases. Meta-analysis is possible for selected topics such as the use of anti-oestrogens in idiopathic oligospermia and unexplained female infertility. Eight cases of double reporting were identified. Conclusions - Trials using randomized methodology were relatively few in comparison with other branches of medicine, although their use is important in the evaluation of treatment for infertility as treatment-independent pregnancy is common. It was encouraging to note that an exponential increase in the use of an unrealistically small sample size, inappropriate use of cross-over design or pseudo-randomization. The trend towards properly controlled studies should be encouraged but these studies should be of improved quality and organised on a multicentre or even international basis.
CC General Biology - Information, Documentation, Retrieval and Computer Applications 00530
Mathematical Biology and Statistical Methods 04500
Pathology, General and Miscellaneous - Therapy *12512
Reproductive System - Pathology *16506
Public Health - Public Health Administration and Statistics *37010
Public Health: Epidemiology - Organic Diseases and Neoplasms *37054

BC Hominidae *86215
IT Major Concepts
Epidemiology (Population Studies); Pathology; Public Health (Allied Medical Sciences); Reproductive System (Reproduction)
IT Miscellaneous Descriptors
COMPUTER LITERATURE REVIEW
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

L1 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2000 ACS
AN 1991:528530 CAPLUS
DN 115:128530
TI Clonidine in determining benefit of growth hormone (GH) or growth hormone releasing-hormone (GHRH) in combination with gonodotropin for treatment of infertility
IN Lunenfeld, Bruno; Menashe, Yeheskel
PA Applied Research Systems Holding N. V. (ARS), Neth.
SO Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM G01N033-74
ICS A61K049-00
CC 2-3 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 421707	A2	19910410	EP 1990-310729	19901001
	EP 421707	A3	19920715		
	EP 421707	B1	19950913		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2026639	AA	19910403	CA 1990-2026639	19901001
	US 5175111	A	19921229	US 1990-592441	19901001
	ES 2077032	T3	19951116	ES 1990-310729	19901001
	IL 95865	A1	19960119	IL 1990-95865	19901001
	AU 9063663	A1	19910411	AU 1990-63663	19901002
	AU 642909	B2	19931104		
	JP 03218467	A2	19910926	JP 1990-264909	19901002
	ZA 9007865	A	19911030	ZA 1990-7865	19901002
PRAI	GB 1989-22137		19891002		

AB Clonidine or a clonidine deriv. is used to det. the level of GH reserve and therefore the likelihood of a female patient to benefit from combined GH/gonadotropin or GHRH/gonadotropin therapy for infertility. The blood level of GH is monitored following administration of the clonidine (deriv.) to det. whether the peak blood level of GH is above a predetd. min. value. A clin. study in which 25 anovulatory patients were administered clonidine-HCl and GH resonses detd. is reported.
ST clonidine growth hormone reserve detn; gonadotropin growth hormone infertility clonidine; infertility growth hormone releasing hormone gonadotropin
IT Gonadotropins
RL: BIOL (Biological study)
(infertility treatment with combination of growth hormone or growth hormone releasing-hormone and, clonidine test for detn. of)
IT Fertility
(female, disorder, treatment of, with combination of gonadotropin and growth hormone or growth hormone releasing hormone, clonidine test for detn. of)
IT 4205-90-7, Clonidine 4205-90-7D, Clonidine, derivs. 4205-91-8, Clonidine hydrochloride
RL: BIOL (Biological study)
(detn. of growth hormone reserve level with, **female infertility treatment** with growth hormone/gonadotropin or growth hormone releasing-hormone/gonadotropin in relation to)
IT 9002-72-6, Growth hormone 9034-39-3, Growth hormone releasing hormone

RL: BIOL (Biological study)
(gonadotropin and, **female infertility treatment** with, clonidine test for detn. of)

IT 61489-71-2, Human menopausal gonadotropin
RL: BIOL (Biological study)
(infertility treatment with combination of growth hormone or growth hormone releasing-hormone and human, clonidine test for detn. of)

L1 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2000 ACS
AN 1991:465552 CAPLUS
DN 115:65552
TI Use of clomiphene for treatment of female infertility
IN Baird, David T.; Glasier, Anna F.
PA Applied Research Systems Holding N. V. (ARS), Neth.
SO Eur. Pat. Appl., 4 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-135
CC 2-3 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 430388	A2	19910605	EP 1990-305063	19900510
	EP 430388	A3	19920219		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2014637	AA	19910520	CA 1990-2014637	19900417

PRAI GB 1989-26171 19891120
AB A method for the treatment of infertility in an anovulatory woman comprises administering to the subject a pharmacol. effective amt. of clomiphene or its bioequiv. deriv. in which the cis isomer is substantially absent. Normoprolactinemic women with regular menstrual cycles and patent Fallopian tubes were treated with 100 g clomiphene citrate daily from day 2 of the first menstrual cycle for 5 days. Pelvic ultrasound scanning indicated that the mean no. of follicles (>16 mm diam.) increased from 1.2 in controls to 2.4. The trans isomer alone, at half the dosage of clomiphene citrate, gave practically the same result.
ST clomiphene **female infertility treatment**
IT Ovulation
(induction of, by clomiphene or its deriv., in infertility treatment)
IT Fertility
(female, disorder, treatment of, with clomiphene, anovulation in relation to)
IT 50-41-9, Clomiphene citrate 911-45-5, Clomiphene 15690-57-0, Enclomiphene
RL: BIOL (Biological study)
(**female infertility treatment** with)

L1 ANSWER 10 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 97:530868 SCISEARCH
GA The Genuine Article (R) Number: XJ757
TI **Female infertility: Treatment** options for complicated cases
AU ANON
SO HUMAN REPRODUCTION, (JUN 1997) Vol. 12, No. 6, pp. 1191-1196.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD, ENGLAND OX2 6DP.
ISSN: 0268-1161.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 76
CC REPRODUCTIVE BIOLOGY; OBSTETRICS & GYNECOLOGY
STP KeyWords Plus (R): POLYCYSTIC-OVARY-SYNDROME; FOLLICLE-STIMULATING-HORMONE; IN-VITRO FERTILIZATION; WOMEN AGE 40; OOCYTE DONATION; OVULATION INDUCTION; OBESE WOMEN; RECURRENT MISCARRIAGE; INVITRO FERTILIZATION; ASSISTED PROCREATION
RF 95-0096 001; IN-VITRO FERTILIZATION; OOCYTE DONATION PROGRAM; NULLIPAROUS WOMEN; OVARIAN RESERVE; MATERNAL AGE; PREGNANCY RATES

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
*REC MISC IMM TRIA	1994	32	55	AM J REPROD IMMUNOL
ABDALLA H I	1993	8	1512	HUM REPROD
AGARWAL S K	1996	65	759	FERTIL STERIL
BAIRD D T	1993		529	OVARY
BENRAFAEL Z	1995	63	689	FERTIL STERIL
BERGA S L	1989	68	301	J CLIN ENDOCR METAB
BORINI A	1995	63	258	FERTIL STERIL
BORINI A	1996	65	94	FERTIL STERIL
BREWIS A A	1993	65	593	HUM BIOL
BUTZOW T L	1996	11	47	HUM REPROD
CANIS M	1991	56	616	FERTIL STERIL
CHEDID S	1995	10	2406	HUM REPROD
CLARK A M	1995	10	2705	HUM REPROD
CLIFFORD K	1994	9	1328	HUM REPROD
COLLINS J A	1989	52	15	FERTIL STERIL
CORSAN G	1996	11	1109	HUM REPROD
CROSIGNANI P G	1994	9	420	HUM REPROD
DEVROEY P	1988	3	699	HUM REPROD
DEVROEY P	1996	11	1324	HUM REPROD
DUBUISSON J B	1990	54	401	FERTIL STERIL
DUBUISSON J B	1991	56	668	FERTIL STERIL
DUBUISSON J B	1994	9	334	HUM REPROD
FARHI J	1995	64	930	FERTIL STERIL
FAUSER B C J M	1993	7	309	BAILLIERE CLIN OB GY
FAYEZ J A	1983	39	476	FERTIL STERIL
FILICORI M	1994	79	1215	J CLIN ENDOCR METAB
FRANKS S	1995	333	853	NEW ENGL J MED
GEBER S	1995	10	1507	HUM REPROD
GOMEL V	1983	40	607	FERTIL STERIL
GRODSTEIN F	1994	5	247	EPIDEMIOLOGY
HAIDL G	1996	11	558	HUM REPROD
HAMER F C	1995	10	1194	HUM REPROD
HAMILTONFAIRLEY D	1990	4	609	BAILLIERE CLIN OB GY

HAMILTONFAIRLEY D	1992	99	128	BRIT J OBSTET GYNAEC
HANSEN L H	1996	11	486	HUM REPROD
HOMBURG R	1989	298	809	BRIT MED J
HOMBURG R	1990	54	737	FERTIL STERIL
HOWE G	1985	290	1697	BRIT MED J
HULL M G R	1996	65	783	FERTIL STERIL
HULL M G R	1992	7	785	HUM REPROD
JACOBS H S	1995	7	203	CURR OPIN OBSTET GYN
KIDDY D S	1990	32	213	CLIN ENDOCRINOL
KIDDY D S	1992	36	105	CLIN ENDOCRINOL
KING C M	1992	4	719	REPROD FERT DEVELOP
LANSAC J	1995	10	1033	HUM REPROD
LETIEXHE M R	1995	80	364	J CLIN ENDOCR METAB
LOBO R A	1995	6	167	ADV ENDOCRINOL METAB
LOBO R A	1991	34	817	CLIN OBSTET GYNECOL
LUTJEN P	1984	307	174	NATURE
MAROULIS G B	1991	9	165	SEMIN REPROD ENDOCR
NAVOT D	1994	61	97	FERTIL STERIL
PADOS G	1994	9	538	HUM REPROD
PASQUALI R	1986	154	139	AM J OBSTET GYNECOL
PEARLSTONE A C	1992	58	674	FERTIL STERIL
PEDERSEN B S	1984	148	140	AM J OBSTET GYNECOL
PELLICER A	1995	10	91	HUM REPROD
RAI R S	1996	11	25	HUM REPROD
SAGLE M A	1991	55	56	FERTIL STERIL
SCHOEMAKER J	1993	7	297	BAILLIERE CLIN OB GY
SCHOOLCRAFT W B	1995	12	581	J ASSIST REPROD GEN
SCHWARTZ D	1982	306	404	NEW ENGL J MED
SCOTT R T	1995	10	1706	HUM REPROD
SIMON C	1994	9	725	HUM REPROD
SMITH K E	1996	65	35	FERTIL STERIL
SPIRA A	1988	1	15	MATURITAS S
STIRRAT G M	1990	336	673	LANCET
STRANDELL A	1994	9	861	HUM REPROD
TORGERSON D J	1996	103	581	BRIT J OBSTET GYNAEC
VANDERSPUY Z M	1988	296	962	BRIT MED J
VANNOORDZAADSTR.BM	1991	302	1361	BRIT MED J
VANSTEIRTEGHEM A C	1992	4	681	REPROD FERT DEVELOP
VERHULST G	1993	8	1284	HUM REPROD
WADE G N	1991	16	235	NEUROSCI BEHAV REV
YEN S S C	1988		231	NEUROENDOCRINOLOGY R
ZAADSTRA B M	1993	306	484	BRIT MED J
ZOUVES C	1991	56	691	FERTIL STERIL

L1 ANSWER 11 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 93:713729 SCISEARCH
GA The Genuine Article (R) Number: MJ181
TI INFERTILITY TREATMENT - FROM COOKERY TO SCIENCE - THE EPIDEMIOLOGY OF RANDOMIZED CONTROLLED TRIALS
AU VANDEKERCKHOVE P; ODONOVAN P A; LILFORD R J (Reprint); HARADA T W
CS UNIV LEEDS, INST EPIDEMIOL & HLTH SERV RES, DEPT CLIN MED, 34 HYDE TERR, LEEDS LS2 9LN, W YORKSHIRE, ENGLAND; TOTTORI UNIV, SCH MED, DEPT OBSTET & GYNAECOL, YONAGO, TOTTORI 683, JAPAN
CYA ENGLAND; JAPAN
SO BRITISH JOURNAL OF OBSTETRICS AND GYNAECOLOGY, (NOV 1993) Vol. 100, No. 11, pp. 1005-1036.
ISSN: 0306-5456.
DT Article; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 323
AB Objectives To review the epidemiology of published randomised controlled trials in infertility treatment over the last 25 years, with special emphasis on the number and quality of trials.

Design Computer literature review by MEDLINE backed up by a manual search of 41 journals. Each trial was classified according to the methodology described and quality criteria. The results were recorded in a computer database. Odds ratios (OR) and confidence intervals (CI) were calculated where the data were sufficient.

Subjects Couples suffering from primary or secondary infertility. The trials studied 33 761 patients overall.

Setting Institute of Epidemiology and Health Services Research, Leeds.

Results Five hundred and one randomised trials in male and **female infertility treatment** were identified between 1966 and 1990. Pregnancy was an outcome in 291 (58%) and these were the subject of detailed analysis. Two hundred and twenty-four (77%) and 67 (23%) 'pregnancy trials' were concerned, respectively, with female and male infertility. Four per cent of the trials were preceded by a sample size calculation, and the average sample size was 96 patients (range 5-933); 700 patients per group would be required to demonstrate plausible success rates for most treatments. The method of randomisation was unstated or pseudo-randomised in 206 (71%) of trials where pregnancy was an outcome. Only 29 (5.8%) of studies were multicentre. The method of confirmation of pregnancy was omitted for 70% of papers. Cross-over design was used in 103 (21%) of cases. Meta-analysis is possible for selected topics such as the use of anti-oestrogens in idiopathic oligospermia and unexplained female infertility. Eight cases of double reporting were identified.

Conclusions Trials using randomised methodology were relatively few in comparison with other branches of medicine, although their use is important in the evaluation of treatment for infertility as treatment-independent pregnancy is common. It was encouraging to note that an exponential increase in the use of this methodology occurred during the last three years, especially in association with assisted conception techniques, and meta-analysis has become possible for selected topics. However, many trials suffer from an unrealistically small sample size, inappropriate use of cross-over design or pseudo-randomisation. The trend towards properly controlled studies should be encouraged but these studies

should be of improved quality and organised on a multicentre or even international basis.

CC OBSTETRICS & GYNECOLOGY

STP KeyWords Plus (R): HUMAN MENOPAUSAL GONADOTROPIN; FOLLICLE-STIMULATING-HORMONE; HUMAN CHORIONIC-GONADOTROPIN; GAMETE INTRAFALLOPIAN TRANSFER; INVITRO FERTILIZATION PROGRAM; POLYCYSTIC OVARIAN DISEASE; UNEXPLAINED PRIMARY INFERTILITY; PLACEBO-CONTROLLED TRIAL; LUTEAL PHASE DEFICIENCY; AGONIST HMG TREATMENT

RF 92-0181 002; SPERM ANTIBODIES; INVITRO FERTILIZATION; ACROSOME REACTION OF HUMAN SPERMATOZOA; SEMINAL QUALITY; TESTICULAR FUNCTION
92-0734 002; METAANALYSIS OF OUTCOME TRIALS; PUBLICATION BIAS; SOCIAL-WORK JOURNALS; ACUTE OTITIS-MEDIA
92-0246 001; INSULIN-LIKE GROWTH FACTOR-BINDING PROTEINS; DIFFERENTIAL EXPRESSION; MODULATING IGF-I ACTION IN BHK CELLS
92-4163 001; INVITRO FERTILIZATION; PREIMPLANTATION GENETIC DIAGNOSIS; LASER MICROMANIPULATION IN THE MOUSE EMBRYO; SUBZONAL SPERM MICROINJECTION; HISTORICAL OVERVIEW
92-4899 001; SYMPTOMATIC ENDOMETRIOSIS; GONADOTROPIN-RELEASING-HORMONE AGONISTS; LEUPROLIDE ACETATE; GNRH ANALOG BUSERELIN
92-5125 001; INVITRO FERTILIZATION; GONADOTROPIN-RELEASING-HORMONE AGONIST; LUTEAL PHASE SUPPORT IN AN IVF GIFT PROGRAM

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
	1982	54	780	BR J UROL
	1984	56	710	BR J UROL
	1983	40	612	FERTIL STERIL
	1989	51	933	FERTIL STERIL
	1989	12	254	INT J ANDROL
AAFJES J H	1983	15	531	ANDROLOGIA
ABDALLA H I	1987	48	958	FERTIL STERIL
ABDALLA H I	1990	53	473	FERTIL STERIL
ABOULGHAR M A	1990	53	311	FERTIL STERIL
AINMELK Y	1982	8	135	ARCH ANDROLOGY
AINMELK Y	1987	48	113	FERTIL STERIL
ALPER M M	1986	68	6	OBSTET GYNECOL
ALTMAN D G	1990	335	149	LANCET
ANNOS T	1980	55	705	OBSTET GYNECOL
ANTOINE J M	1990	5	565	HUM REPROD
ARCHER D F	1986	46	1037	FERTIL STERIL
ASHKENAZI J	1989	30	157	EUR J OBSTET GYN R B
BABER R	1988	14	453	ASIA OCEANIA J OBSTE
BACHUS K E	1990	54	27	FERTIL STERIL
BAERTHLEIN W	1988	71	277	OBSTET GYNECOL
BAKER H W G	1984	7	383	INT J ANDROL
BALASCH J	1982	37	751	FERTIL STERIL
BARASH A	1990	53	865	FERTIL STERIL
BARRATT C L R	1989	52	394	FERTIL STERIL
BAYER S R	1988	33	179	J REPROD MED
BEDFORD N	1981		339	DIAGNOSIS TREATMENT
BELAISCHALLART J	1987	2	183	HUM REPROD
BELAISCHALLART J	1990	5	163	HUM REPROD
BELAISCHALLART J	1990	5	573	HUM REPROD
BELLINGE B S	1986	46	252	FERTIL STERIL
BENADIVA C A	1988	50	777	FERTIL STERIL

BENADIVA C A	1989	6	164	J IN VITRO FERTIL EM
BENEDEKJASZMANN L	1976	22	1095	LANCET
BENTICK B	1988	50	79	FERTIL STERIL
BERGER M	1971	22	787	FERTIL STERIL
BERGQUIST C	1990	162	589	AM J OBSTET GYNECOL
BHATHENA R	1986	23	244	HORM RES
BHATHENA R	1987	332	306	INT J FERTIL
BIBEROGLU K O	1981	139	645	AM J OBSTET GYNECOL
BLUMENFELD Z	1988	50	403	FERTIL STERIL
BLUMENFELD Z	1989	51	863	FERTIL STERIL
BRESLOW N E	1980	1	142	STATISTICAL METHODS
BRINSMEAD M	1989	6	149	J IN VITRO FERTIL EM
BROWN C A	1988	50	825	FERTIL STERIL
BURRY K A	1989	160	1454	AM J OBSTET GYNECOL
BUVAT J	1988	49	458	FERTIL STERIL
BUVAT J	1989	52	553	FERTIL STERIL
BUVAT J	1990	53	490	FERTIL STERIL
BUVAT J	1987	28	219	HORM RES
BUVAT J	1990	53	521	FERTIL STERIL
BYRD W	1990	19	96	J GYNECOL OBST BIO R
CABAU A	1986	3	215	J IN VITRO FERTIL EM
CARO C M	1983	2	1191	LANCET
CASPER R F	1989	52	146	FERTIL STERIL
CASPI E	1989		15	EFFECTIVE CARE PREGN
CHALMERS I	1989	6	275	J IN VITRO FERTIL EM
CHANG S Y	1988	3	252	INT J FERTIL
CHECK J	1989	34	120	INT J FERTIL
CHECK J H	1989	34	209	INT J FERTIL
CHECK J H	1989	34	1021	J REPROD MED
CLAESSON B	1989	18	1049	J GYNECOL OBST BIO R
CLARAZ E	1989	10	240	J ANDROL
CLARK R V	1989	1		EFFECTIVE CARE PREGN
COCHRANE A	1979		1	MED YEAR 2000
COCHRANE A	1990	53	662	FERTIL STERIL
COHEN J	1990	5	7	HUM REPROD
COHEN J	1986	17	279	ACTA EUR FERTIL
COLPI G	1986	17	121	ACTA EUR FERTIL
COLPI G M	1990	54	689	FERTIL STERIL
COMHAIRE F	1986	9	91	INT J ANDROL
COMHAIRE F H	1977	28	1211	FERTIL STERIL
COMNINOS A	1974	43	697	OBSTET GYNECOL
CONNAUGHTON J	1989	1	27	ACTA OBSTET GYNECO S
COOKE I	1987	16	227	CONTR GYNECOL OBSTET
COUTINHO E	1986	46	673	FERTIL STERIL
CRUZ R I	1966	17	363	FERTIL STERIL
CUDMORE D	1986	3	326	J IN VITRO FERTIL EM
CUMMINS J M	1984	41	844	FERTIL STERIL
DALY D C	1990	5	138	HUM REPROD
DAURES J P	1985	8	111	INT J ANDROL
DEALMEIDA M	1990	54	1083	FERTIL STERIL
DEATON J L	1988	28	65	EUR J OBSTET GYN R B
DEBOER A D	1981	35	162	FERTIL STERIL
DECHERNEY A H	1969	20	373	FERTIL STERIL
DENBER H	1988	49	913	FERTIL STERIL
DLUGI A M	1989	51	395	FERTIL STERIL
DMOWSKI W P	1982	59	408	OBSTET GYNECOL
DMOWSKI W P	1987	65	65	J CLIN ENDOCR METAB
DODSON W	1989	52	915	FERTIL STERIL
DODSON W C				

EASTERBROOK P J	1991	337	867	LANCET
ECHT C	1969	20	564	FERTIL STERIL
EDELSTEIN M C	1990	53	103	FERTIL STERIL
ELSTEIN M	1984	109	173	CIBA F SYMP
ENGLERT Y	1986	3	243	J IN VITRO FERTIL EM
EVERHARDT E	1990	5	133	HUM REPROD
FAKIH H	1990	53	515	FERTIL STERIL
FEDELE L	1989	161	871	AM J OBSTET GYNECOL
FEDELE L	1989	51	781	FERTIL STERIL
FEDELE L	1990	76	79	OBSTET GYNECOL
FEDERMAN C A	1990	54	489	FERTIL STERIL
FEICHTINGER W	1986	3	87	J IN VITRO FERTIL EM
FELDBERG D	1990	34	103	EUR J OBSTET GYN R B
FERRIER A	1990	54	90	FERTIL STERIL
FISCH B	1989	4	954	HUM REPROD
FISCH P	1989	51	828	FERTIL STERIL
FISHEL S	1987	4	260	J IN VITRO FERTIL EM
FRANCAVILLA F	1985	16	411	ACTA EUR FERTIL
FREDRICSSON B	1981	11	319	EUR J OBSTET GYN R B
FRIBERG J	1973	116	330	AM J OBSTET GYNECOL
FRIBERG J	1977	22	148	INT J FERTIL
FRIEDMAN A	1989	34	199	INT J FERTIL
FRYDMAN R	1988	50	471	FERTIL STERIL
FRYDMAN R	1988	3	559	HUM REPROD
GADIR A A	1990	32	749	CLIN ENDOCRINOL
GADIR A A	1990	33	585	CLIN ENDOCRINOL
GARCIA C R	1985	44	478	FERTIL STERIL
GARCIA J E	1990	53	302	FERTIL STERIL
GERHARD I	1990	24	129	ARCH ANDROLOGY
GIANAROLI L	1989	6	213	J IN VITRO FERTIL EM
GINDOFF P R	1990	7	94	J IN VITRO FERTIL EM
GIOVENCO P	1987	19	238	ANDROLOGIA
GLASIER A F	1989	4	252	HUM REPROD
GLAZENER C	1987	1	373	GYNECOL ENDOCRINOL
GLAZENER C M A	1987	94	774	BRIT J OBSTET GYNAEC
GLAZENER C M A	1990	4	75	GYNECOL ENDOCRINOL
GOLDMAN J	1969	20	393	FERTIL STERIL
GONEN Y	1990	71	918	J CLIN ENDOCR METAB
HAAS G G	1987	47	295	FERTIL STERIL
HARRISON R	1979		209	LANCET 0127
HARRISON R	1975		605	LANCET 0315
HARRISON R F	1983	76	273	IRISH MED J
HARRY J D	1988	3	173	PHARM MED
HENDRY W F	1990	335	85	LANCET
HENZL M	1989	34	1025	J REPROD MED
HENZL M R	1990	162	570	AM J OBSTET GYNECOL
HENZL M R	1988	318	485	NEW ENGL J MED
HERMAN A	1990	53	92	FERTIL STERIL
HILLS M	1979	8	7	BRIT J CLIN PHARMACO
HINTON R	1979	86	379	BRIT J OBSTET GYNAEC
HO P C	1989	51	682	FERTIL STERIL
HOFFMAN D I	1985	60	922	J CLIN ENDOCR METAB
HOGERZEIL H V	1988	49	1030	FERTIL STERIL
HOMBURG R	1990	53	254	FERTIL STERIL
HOMBURG R	1990	54	737	FERTIL STERIL
HOMBURG R	1990	5	32	HUM REPROD
HORNSTEIN M D	1990	53	237	FERTIL STERIL
HOVATTA O	1979	11	377	CLIN ENDOCRINOL

HOVATTA O	1990	54	339	FERTIL STERIL
HUANG K E	1986	155	824	AM J OBSTET GYNECOL
HUANG K E	1984	64	32	OBSTET GYNECOL
HUGHES E G	1987	48	278	FERTIL STERIL
IDDENDEN D A	1985	30	54	INT J FERTIL
IFFLAND C A	1989	32	115	EUR J OBSTET GYN R B
IMOEDEMHE D A G	1987	94	889	BRIT J OBSTET GYNAEC
IRVINE D S	1986	2	972	LANCET
IZZO P L	1984	16	156	ANDROLOGIA
JANSEN R P S	1985	153	363	AM J OBSTET GYNECOL
JANSSENCASPERS H	1988	3	337	HUM REPROD
JOHNSON J	1966	11	265	INT J FERTIL
JOHNSON P	1990	300	154	BRIT MED J
KATAYAMA K P	1979	135	207	AM J OBSTET GYNECOL
KATZ M	1980	1	1306	LANCET
KAUPPILA A	1989	150	7	ACTA OBSTET GYNECO S
KAUPPILA A	1988	49	37	FERTIL STERIL
KEMETER P	1986	1	441	HUM REPROD
KENNEDY S H	1990	53	998	FERTIL STERIL
KENNEDY S H	1990	75	914	OBSTET GYNECOL
KERIN J F P	1984	1	533	LANCET
KHAN I	1989	4	323	HUM REPROD
KHAN I	1989	4	921	HUM REPROD
KUBIK C J	1990	54	836	FERTIL STERIL
KUPFERMINC M J	1990	5	271	HUM REPROD
LARSEN T	1990	53	426	FERTIL STERIL
LARSSON B	1985	64	437	ACTA OBSTET GYN SCAN
LAUFER N	1984	42	198	FERTIL STERIL
LAVY G	1988	50	74	FERTIL STERIL
LEETON J	1987	48	605	FERTIL STERIL
LEETON J	1985	2	166	J IN VITRO FERTIL EM
LEHTINEN A M	1987	4	23	J IN VITRO FERTIL EM
LEONG M	1988	3	877	HUM REPROD
LEWIN A	1985	151	621	AM J OBSTET GYNECOL
LEWIN A	1986	46	257	FERTIL STERIL
LEWIN A	1989	6	139	J IN VITRO FERTIL EM
LEYENDECKER G	1990	5	52	HUM REPROD
LILFORD R J	1987	295	1298	BRIT MED J
LILFORD R J	1987	295	155	BRIT MED J
LILFORD R J	1990	322	780	NEW ENGL J MED
LIPITZ S	1989	28	31	GYNECOL OBSTET INVES
LOUMAYE E	1989	51	105	FERTIL STERIL
LUISI M	1982	2	47	LANCET
LUNGLMAYR G	1983	15	548	ANDROLOGIA
MACLENNAN A H	1985	25	68	AUST NZ J OBSTET GYN
MAHADEVAN M M	1987	47	976	FERTIL STERIL
MAHADEVAN M M	1985	2	190	J IN VITRO FERTIL EM
MANSOUR R	1990	54	678	FERTIL STERIL
MARCONI G	1989	51	357	FERTIL STERIL
MARTINEZ A R	1990	53	847	FERTIL STERIL
MASHIACH S	1989	3	107	GYNECOL ENDOCRINOL
MAVROUDIS K	1987	1	177	GYNECOL ENDOCRINOL
MCBAIN J	1986	87	5	BRIT J OBSTET GYNAEC
MCBAIN J	1982	1	145	CLIN REPROD FERTIL
MCFAUL P	1989	20	157	ACTA EUR FERTIL
MCFAUL P B	1990	53	792	FERTIL STERIL
MCFAUL P B	1989	34	194	INT J FERTIL
MELIS G B	1987	47	441	FERTIL STERIL

MENEZO Y	1989	52	680	FERTIL STERIL
MESSINIS I E	1987	79	549	J REPROD FERTIL
MICIC S	1985	16	51	ACTA EUR FERTIL
MICIC S	1988	19	135	ACTA EUR FERTIL
MICIC S	1988	20	55	ANDROLOGIA
MICIC S	1990	22	179	ANDROLOGIA
MICIC S	1985	133	221	J UROLOGY
MITCHELL J D	1989	6	263	J IN VITRO FERTIL EM
MIYAKE A	1987	26	19	EUR J OBSTET GYN R B
MOORE E E	1981	36	15	FERTIL STERIL
MORRIS J A	1988	296	1313	BRIT MED J
NADER S	1988	5	81	J IN VITRO FERTIL EM
NEVEU S	1987	47	639	FERTIL STERIL
NEVUE S	1986	15	799	J GYNECOL OBST BIO R
NILSSON S	1979	51	591	BR J UROL
NOBLE A D	1980	87	726	BRIT J OBSTET GYNAEC
NOWROOZI K	1987	32	442	INT J FERTIL
ODONOVAN P	1993	8		IN PRESS HUMAN REPRO
OLIVE D L	1986	45	157	FERTIL STERIL
ONEILL C	1985	2	615	LANCET
ONEILL C	1989	2	769	LANCET
PAINVAIN E	1989	20	91	ACTA EUR FERTIL
PAMPIGLIONE J S	1988	50	603	FERTIL STERIL
PARINAUD J	1987	24	285	EUR J OBSTET GYN R B
PARINAUD J	1987	25	203	EUR J OBSTET GYN R B
PATTON P E	1990	5	263	HUM REPROD
PAULSON D	1979	121	432	J UROLOGY
PELLICER A	1989	4	285	HUM REPROD
PHILIPP E	1987	295	610	BRIT MED J
POLAN M L	1986	63	1284	J CLIN ENDOCR METAB
POLIAK A	1973	24	921	FERTIL STERIL
PORTER R	1984		1284	LANCET
PRYOR J	1978	50	47	BR J UROL
PSALTI I	1989	52	807	FERTIL STERIL
PUSCH H H	1989	21	76	ANDROLOGIA
QUARTERO H W P	1989	4	247	HUM REPROD
QUERLEU D	1989	18	935	J GYNECOL OBST BIO R
QUIGLEY M M	1984	42	25	FERTIL STERIL
QUIGLEY M M	1988	50	562	FERTIL STERIL
QUINN P	1990	53	168	FERTIL STERIL
RABINOWITZ R	1989	3	117	GYNECOL ENDOCRINOL
RANOUX C	1990	7	6	J IN VITRO FERTIL EM
REMOHI J	1989	4	918	HUM REPROD
REMORGIDA V	1989	6	76	J IN VITRO FERTIL EM
RICHTER M A	1984	41	277	FERTIL STERIL
RIZK B	1990	54	661	FERTIL STERIL
ROCK J A	1984	41	229	FERTIL STERIL
ROCK J A	1984	42	373	FERTIL STERIL
ROLLAND R	1990	1162	586	AM J OBSTET GYNECOL
RONEL R	1990	54	233	FERTIL STERIL
RONNBERG L	1980	3	479	INT J ANDROL
ROSSMANITH W G	1987	32	460	INT J FERTIL
ROUMEN F J M E	1984	41	237	FERTIL STERIL
SALATBAROUX J	1988	3	331	HUM REPROD
SALATBAROUX J	1988	3	535	HUM REPROD
SALATBAROUX J	1988	5	153	J IN VITRO FERTIL EM
SCHILL W B	1981	31	121	ANDROLOGIA
SCHILL W B	1979	2	163	ARCH ANDROLOGY

SCHMIDT C L	1985	44	157	FERTIL STERIL
SCHWABE M G	1983	40	604	FERTIL STERIL
SCOCCIA B	1987	48	446	FERTIL STERIL
SEIBEL M M	1982	38	534	FERTIL STERIL
SEIBEL M M	1985	43	703	FERTIL STERIL
SEILER J C	1986	46	1098	FERTIL STERIL
SEMCZUK M	1985	17	131	MATERIA MED POLONA
SHARLIP I D	1981	17	347	UROLOGY
SHARMA V	1989	51	298	FERTIL STERIL
SHAW R	1987	5	141	CLIN REPROD FERTIL
SHAW R W	1990	162	574	AM J OBSTET GYNECOL
SMITH E M	1989	298	1483	BRIT MED J
SMITZ J	1988	3	585	HUM REPROD
SOIHET M	1974	19	111	INT J FERTIL
SOKOL R Z	1988	49	865	FERTIL STERIL
SOPELAK V M	1989	52	627	FERTIL STERIL
STAEMMLER H	1966	14	818	WEIN KLIN WOCHENSCHR
STAESSEN C	1990	5	336	HUM REPROD
STARUP J	1972	71	469	ACTA ENDOCRINOL-COP
STEINBERGER E	1973	223	778	JAMA-J AM MED ASSOC
SUELDO C E	1986	45	128	FERTIL STERIL
SUTARIA U	1980	18	435	J GYNECOL OBSTET
SWOLIN K	1967	46	204	ACTA OBSTET GYNEC SC
TAL J	1985	44	342	FERTIL STERIL
TANBO T	1990	53	798	FERTIL STERIL
TANBO T	1990	5	811	HUM REPROD
TANBO T	1990	5	266	HUM REPROD
TANPHAICHITR N	1988	5	119	J IN VITRO FERTIL EM
TELIMAA S	1988	50	872	FERTIL STERIL
TELIMAA S	1987	1	363	GYNECOL ENDOCRINOL
TEVELDE E R	1989	51	182	FERTIL STERIL
THOMAS E J	1987	294	1117	BRIT MED J
THOMAS E J	1987	294	272	BRIT MED J
THORNTON S J	1990	53	177	FERTIL STERIL
TORODE H	1987	5	255	CLIN REPROD FERTIL
TOROK L	1985	17	497	ANDROLOGIA
TROUNSON A	1986	45	532	FERTIL STERIL
TROUNSON A O	1982	64	285	J REPROD FERTIL
TULANDI T	1985	44	846	FERTIL STERIL
TULANDI T	1986	45	489	FERTIL STERIL
TULANDI T	1989	52	421	FERTIL STERIL
TUMMON I S	1989	51	390	FERTIL STERIL
VALIMAKI M	1989	69	1097	J CLIN ENDOCR METAB
VANDEHELDER A B	1990	7	358	J IN VITRO FERTIL EM
VANDERVEN H	1988	3	81	HUM REPROD S2
VANDIJK J	1979	55	79	POSTGRADUATE J ME S5
VANDIJK J G	1979	31	481	FERTIL STERIL
VANOS H	1989	52	360	FERTIL STERIL
VANSTEIRTEGHEM A C	1988	3	161	HUM REPROD
VARGYAS J M	1984	42	745	FERTIL STERIL
VERE M F	1979	2	100	BRIT MED J
WANG C	1983	40	358	FERTIL STERIL
WIELAND R	1972	23	471	FERTIL STERIL
WIKLAND M	1987	2	191	HUM REPROD
WISANTO A	1989	52	79	FERTIL STERIL
WONG Y F	1990	2	351	REPROD FERT DEVELOP
WRIGHT C S	1979	1	1037	BRIT MED J
WU C H	1989	52	564	FERTIL STERIL

YLIKORKALA O	1990	4	251	GYNECOL ENDOCRINOL
YOVICH J L	1984	24	125	AUST NZ J OBSTET GYN

L1 ANSWER 12 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 80:518578 SCISEARCH
GA The Genuine Article (R) Number: KS851
TI MICRO-SURGERY IN **FEMALE INFERTILITY TREATMENT**
AU FLOERSHEIM Y (Reprint)
CS UNIV ZURICH, KANTONSSPITAL, DEPT FRAUENHEILKUNDE, ENDOKRINOL ABT, CH-8091 ZURICH, SWITZERLAND (Reprint)
CYA SWITZERLAND
SO SCHWEIZERISCHE RUNDSCHAU FUR MEDIZIN PRAXIS, (1980) Vol. 69, No. 48, pp. 1780-1785.
DT Article; Journal
FS CLIN
LA German
REC No References
Keyed
CC MEDICINE, GENERAL & INTERNAL

```
=> s TGFbeta and fertility treatment
L2            0 TGFBETA AND FERTILITY TREATMENT
=> s TGF beta
L3        66383 TGF BETA
=> s l3 and sperm antigen
L4            1 L3 AND SPERM ANTIGEN
=> d 14 all
```

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
AN 1998:618828 CAPLUS
DN 129:212101
TI Treatment and diagnosis of infertility using **TGF.beta.** or activin
IN Robertson, Sarah Anne; Tremellen, Kelton Paul
PA Luminis Pty. Ltd., Australia
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-18
ICS A61K039-00; G01N033-68
CC 2-3 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9839021	A1	19980911	WO 1998-AU149	19980306
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9862846	A1	19980922	AU 1998-62846	19980306
	AU 722150	B2	20000720		
	EP 1028743	A1	20000823	EP 1998-906749	19980306
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI AU 1997-5508 19970306
WO 1998-AU149 19980306

AB A method of treating an infertility condition in humans or mammals, by exposure of a prospective mother to **TGF.beta.** or a deriv. or analog of **TGF.beta.**. The exposure is advantageously in conjunction with one or more antigens of a prospective father so that a hyporesponsive immune reaction is mounted to the one or more antigens of the prospective father. The treatment illicts a transient hyporesponsive immune reaction that alleviates symptoms of the infertility condition. Methods are also claimed for diagnosing an infertility condition in males by testing the level of **TGF.beta.** in the seminal fluid and in females by testing for the capacity of the female to convert the inactive form of **TGF.beta.** to the active form. Some specific disorders or procedures that may benefit from the present invention are: recurrent miscarriage, IVF treatment, anti-sperm antibody therapy, pre-eclampsia and intra-uterine growth restriction, prospective anal. of stud animal fertility in livestock breeding industries, and optimization of pregnancy outcome in livestock breeding industries.

ST infertility treatment diagnosis TGFbeta activin; paternal antigen TGFbeta infertility treatment diagnosis

IT Platelet (blood)
(**TGF.beta.** administration in the form of platelets; treatment and diagnosis of infertility using **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father)

IT Antibodies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-sperm antibody therapy; treatment and diagnosis of infertility using **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Semen
Seminal plasma
(antigen administration in; treatment and diagnosis of infertility using **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father)

IT Leukocyte
Sperm
(**antigen** administration on; treatment and diagnosis of infertility using **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father)

IT Livestock
(breeding; treatment and diagnosis of infertility using **TGF .beta.** or activin in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Transforming growth factors .beta.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs. or analogs; treatment and diagnosis of infertility using **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father)

IT Uterine diseases
(intra-uterine growth restriction; treatment and diagnosis of infertility using **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Breeding (animal)
(livestock; treatment and diagnosis of infertility using **TGF .beta.** or activin in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Diagnosis
Infertility (animal)
(treatment and diagnosis of infertility using **TGF .beta.** or activin in conjunction with one or more antigens of a prospective father)

IT Antigens
Class I MHC antigens
MHC antigens
Transforming growth factor .beta.1
Transforming growth factor .beta.2
Transforming growth factor .beta.3
Transforming growth factors .beta.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment and diagnosis of infertility using **TGF .beta.** or activin in conjunction with one or more antigens of a prospective father)

IT Abortion (spontaneous)
In vitro fertilization (animal)
Preeclampsia
(treatment and diagnosis of infertility using **TGF .beta.** or activin in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Drug delivery systems

Vaginal drug delivery systems
(treatment and diagnosis of infertility using compns. contg. **TGF.beta.** or activin in conjunction with one or more antigens of a prospective father)

```
=> s activin and infertility treatment
L5              1 ACTIVIN AND INFERTILITY TREATMENT
=> d 15 all
```

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
AN 1998:618828 CAPLUS
DN 129:212101
TI Treatment and diagnosis of infertility using TGF.beta. or **activin**
IN Robertson, Sarah Anne; Tremellen, Kelton Paul
PA Luminis Pty. Ltd., Australia
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9839021	A1	19980911	WO 1998-AU149	19980306
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9862846	A1	19980922	AU 1998-62846	19980306
	AU 722150	B2	20000720		
	EP 1028743	A1	20000823	EP 1998-906749	19980306
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI AU 1997-5508 19970306
WO 1998-AU149 19980306

AB A method of treating an infertility condition in humans or mammals, by exposure of a prospective mother to TGF.beta. or a deriv. or analog of TGF.beta.. The exposure is advantageously in conjunction with one or more antigens of a prospective father so that a hyporesponsive immune reaction is mounted to the one or more antigens of the prospective father. The treatment illicts a transient hyporesponsive immune reaction that alleviates symptoms of the infertility condition. Methods are also claimed for diagnosing an infertility condition in males by testing the level of TGF.beta. in the seminal fluid and in females by testing for the capacity of the female to convert the inactive form of TGF.beta. to the active form. Some specific disorders or procedures that may benefit from the present invention are: recurrent miscarriage, IVF treatment, anti-sperm antibody therapy, pre-eclampsia and intra-uterine growth restriction, prospective anal. of stud animal fertility in livestock breeding industries, and optimization of pregnancy outcome in livestock breeding industries.

ST **infertility treatment** diagnosis TGFbeta **activin**; paternal antigen TGFbeta **infertility treatment** diagnosis

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IT Leukocyte
Sperm
(antigen administration on; treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father)

IT Livestock
(breeding; treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Transforming growth factors .beta.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs. or analogs; treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father)

IT Uterine diseases
(intra-uterine growth restriction; treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Breeding (animal)
(livestock; treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Diagnosis
Infertility (animal)
(treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father)

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MHC antigens
Transforming growth factor .beta.1
Transforming growth factor .beta.2
Transforming growth factor .beta.3
Transforming growth factors .beta.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father)

IT Abortion (spontaneous)
In vitro fertilization (animal)
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(treatment and diagnosis of infertility using TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father to benefit various disorders and procedures)

IT Drug delivery systems
Vaginal drug delivery systems

(treatment and diagnosis of infertility using compns. contg. TGF.beta. or **activin** in conjunction with one or more antigens of a prospective father)

```
=> s transforming growth factor beta 1 and female reproduction

   4 FILES SEARCHED...
L6            0 TRANSFORMING GROWTH FACTOR BETA 1 AND FEMALE REPRODUCTION

=> s TGF beta and reproduction

L7         1025 TGF BETA AND REPRODUCTION

=> s l7 and infertility

L8           17 L7 AND INFERTILITY

=> d l8 all 1-17
```

L8 ANSWER 1 OF 17 MEDLINE
AN 1999306568 MEDLINE
DN 99306568
TI Paracrine actions of growth differentiation factor-9 in the mammalian ovary.
AU Elvin J A; Clark A T; Wang P; Wolfman N M; Matzuk M M
CS Department of Pathology, Baylor College of Medicine, Houston, Texas 77030, USA.
NC HD-33438 (NICHD)
GM-07330 (NIGMS)
GM-08307 (NIGMS)
SO MOLECULAR ENDOCRINOLOGY, (1999 Jun) 13 (6) 1035-48.
Journal code: NGZ. ISSN: 0888-8809.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
AB Although the transforming growth factor-beta (**TGF-beta**) superfamily is the largest family of secreted growth factors, surprisingly few downstream target genes in their signaling pathways have been identified. Likewise, the identities of oocyte-derived secreted factors, which regulate important oocyte-somatic cell interactions, remain largely unknown. For example, oocytes are known to secrete paracrine growth factor(s) which are necessary for cumulus expansion, induction of hyaluronic acid synthesis, and suppression of LH receptor (LHR) mRNA synthesis. Our previous studies demonstrated that absence of the **TGF-beta** family member, growth differentiation factor-9 (GDF-9), blocks ovarian folliculogenesis at the primary follicle stage leading to **infertility**. In the present study, we demonstrate that mouse GDF-9 protein is expressed in all oocytes beginning at the type 3a follicle stage including antral follicles. To explore the biological functions of GDF-9 in the later stages of folliculogenesis and cumulus expansion, we produced mature, glycosylated, recombinant mouse GDF-9 using a Chinese hamster ovary cell expression system. A granulosa cell culture system was established to determine the role of GDF-9 in the regulation of several key ovarian gene products using semiquantitative RT-PCR. We find that recombinant GDF-9 induces hyaluronan synthase 2 (HAS2), cyclooxygenase 2 (COX-2), and steroidogenic acute regulator protein (StAR) mRNA synthesis but suppresses urokinase plasminogen activator (uPA) and LHR mRNA synthesis. Consistent with the induction of StAR mRNA by GDF-9, recombinant GDF-9 increases granulosa cell progesterone synthesis in the absence of FSH. Since induction of HAS2 and suppression of the protease uPA in cumulus cells are key events in the production of the hyaluronic acid-rich extracellular matrix which is produced during cumulus expansion, we determined whether GDF-9 could mimic this process. Using oocytectomized cumulus cell-oocyte complexes, we show that recombinant GDF-9 induces cumulus expansion in vitro. These studies demonstrate that GDF-9 can bind to receptors on granulosa cells to regulate the expression of a number of gene products. Thus, in addition to playing a critical function as a

growth and differentiation factor during early folliculogenesis, GDF-9 functions as an oocyte-secreted paracrine factor to regulate several key granulosa cell enzymes involved in cumulus expansion and maintenance of an optimal oocyte microenvironment, processes which are essential for normal ovulation, fertilization, and female **reproduction**.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
CHO Cells
FSH: ME, metabolism
FSH: PD, pharmacology
Glucuronosyltransferase: DE, drug effects
Glucuronosyltransferase: GE, genetics
Granulosa Cells: ME, metabolism
Growth Substances: GE, genetics
*Growth Substances: ME, metabolism
Growth Substances: PD, pharmacology
Hamsters
Immunohistochemistry
Isoenzymes: DE, drug effects
Isoenzymes: GE, genetics
Isoenzymes: ME, metabolism
Mice
Mice, Inbred ICR
*Ovary: ME, metabolism
*Paracrine Communication: PH, physiology
Phosphoproteins: DE, drug effects
Phosphoproteins: GE, genetics
Phosphoproteins: ME, metabolism
Progesterone: BI, biosynthesis
Prostaglandin-Endoperoxide Synthase: DE, drug effects
Prostaglandin-Endoperoxide Synthase: GE, genetics
Prostaglandin-Endoperoxide Synthase: ME, metabolism
Receptors, LH: DE, drug effects
Receptors, LH: GE, genetics
Recombinant Proteins: GE, genetics
Recombinant Proteins: ME, metabolism
Recombinant Proteins: PD, pharmacology
RNA, Messenger
Urinary Plasminogen Activator: DE, drug effects
Urinary Plasminogen Activator: GE, genetics
Urinary Plasminogen Activator: ME, metabolism

RN 57-83-0 (Progesterone); 9002-68-0 (FSH)

CN EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase); EC 2.4.1.- (Has2 protein, mouse); EC 2.4.1.17 (Glucuronosyltransferase); EC 3.4.21.73 (Urinary Plasminogen Activator); 0 (growth differentiation factor 9); 0 (steroidogenic acute regulatory protein); 0 (Growth Substances); 0 (Isoenzymes); 0 (Phosphoproteins); 0 (Receptors, LH); 0 (Recombinant Proteins); 0 (RNA, Messenger)

L8 ANSWER 2 OF 17 MEDLINE
AN 96298436 MEDLINE
DN 96298436
TI Changes in NK activities and **TGF- beta** concentrations in the peritoneal cavity in endometriosis and their interaction related with **infertility**.
AU Mizumoto Y
CS Department of Obstetrics and Gynecology, National Defense Medical College, Saitama.
SO NIPPON SANKA FUJINKA GAKKAI ZASSHI. ACTA OBSTETRICA ET GYNAECOLOGICA JAPONICA, (1996 Jun) 48 (6) 379-85. Journal code: INR. ISSN: 0300-9165.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 199702
EW 19970204
AB The purpose of this study was to clarify the relationship between NK activity and TG-beta in the immune system in endometriosis. We investigated (1) the changes in the NK activity and concentration of **TGF-beta** in human peritoneal fluid (HPF), and (2) the effects of HPF and **TGF-beta** on the development of early mice embryos. In a rat model of experimental endometriosis, we observed the effects of tissue culture supernatants of peritoneum on NK activity in rat spleen cells, and obtained the following results. (1) NK activity of peripheral lymphocytes in healthy women was significantly suppressed in the presence of HPF of endometriosis. (2) The concentrations of **TGF-beta** was significantly higher in HPF of endometriosis than in HPF of healthy women. (3) Both HPF of endometriosis and **TGF-beta** significantly inhibited the development of early mice embryos. (4) The supernatants prepared from the intact peritoneum of the rat model showed marked inhibition of NK activity compared to control rats, although the peritoneum was obtained from a region distant from the implanted endometrium. These results suggest that ectopic endometrial tissues may cause a change in the cell-mediated immune system and subsequently exert an adverse effect on human **reproduction**.
CT Check Tags: Animal; Female; Human; In Vitro
*Ascitic Fluid: IM, immunology
Ascitic Fluid: ME, metabolism
Cells, Cultured
*Endometriosis: IM, immunology
*Endometriosis: ME, metabolism
Endometrium: ME, metabolism
English Abstract
Fetal Development
***Infertility, Female: ET, etiology**
*Killer Cells, Natural: IM, immunology
Mice
Mice, Inbred ICR
Rats
Rats, Wistar
*Transforming Growth Factor beta: ME, metabolism
*Transforming Growth Factor beta: PH, physiology

CN 0 (Transforming Growth Factor beta)

L8 ANSWER 3 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 2000297153 EMBASE
TI Paracrine actions of growth differentiation factor-9 in the mammalian ovary.
AU Elvin J.A.; Clark A.T.; Wang P.; Wolfman N.M.; Matzuk M.M.
CS Dr. M.M. Matzuk, Department of Pathology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States. mmatzuk@bcm.tmc.edu
SO Molecular Endocrinology, (1999) 13/6 (1035-1048).
Refs: 48
ISSN: 0888-8809 CODEN: MOENEN
CY United States
DT Journal; Article
FS 003 Endocrinology
021 Developmental Biology and Teratology
LA English
SL English
AB Although the transforming growth factor-.beta. (**TGF**-.**beta**.) superfamily is the largest family of secreted growth factors, surprisingly few downstream target genes in their signaling pathways have been identified. Likewise, the identities of oocyte-derived secreted factors, which regulate important oocyte-somatic cell interactions, remain largely unknown. For example, oocytes are known to secrete paracrine growth factor(s) which are necessary for cumulus expansion, induction of hyaluronic acid synthesis, and suppression of LH receptor (LHR) mRNA synthesis. Our previous studies demonstrated that absence of the **TGF**-.**beta**. family member, growth differentiation factor-9 (GDF-9), blocks ovarian folliculogenesis at the primary follicle stage leading to **infertility**. In the present study, we demonstrate that mouse GDF-9 protein is expressed in all oocytes beginning at the type 3a follicle stage including antral follicles. To explore the biological functions of GDF-9 in the later stages of folliculogenesis and cumulus expansion, we produced mature, glycosylated, recombinant mouse GDF-9 using a Chinese hamster ovary cell expression system. A granulosa cell culture system was established to determine the role of GDF-9 in the regulation of several key ovarian gene products using semiquantitative RT-PCR. We find that recombinant GDF-9 induces hyaluronan synthase 2 (HAS2), cyclooxygenase 2 (COX-2), and steroidogenic acute regulator protein (StAR) mRNA synthesis but suppresses urokinase plasminogen activator (uPA) and LHR mRNA synthesis. Consistent with the induction of StAR mRNA by GDF-9, recombinant GDF-9 increases granulosa cell progesterone synthesis in the absence of FSH. Since induction of HAS2 and suppression of the protease uPA in cumulus cells are key events in the production of the hyaluronic acid-rich extracellular matrix which is produced during cumulus expansion, we determined whether GDF-9 could mimic this process. Using oocytectomized cumulus cell-oocyte complexes, we show that recombinant GDF-9 induces cumulus expansion in vitro. These studies demonstrate that GDF-9 can bind to receptors on granulosa cells to regulate the expression of a number of gene products. Thus, in addition to playing a critical function as a growth and differentiation factor during early folliculogenesis, GDF-9 functions as an oocyte-secreted paracrine factor to regulate several key granulosa cell enzymes involved in cumulus

expansion and maintenance of an optimal oocyte microenvironment, processes
which are essential for normal ovulation, fertilization, and female **reproduction**.

CT Medical Descriptors:
*paracrine signaling
*ovary follicle development
*gene targeting
mammal
CHO cell
enzyme activity
granulosa cell
ovulation
fertilization
cumulus oophorus
protein expression
amino acid synthesis
reverse transcription polymerase chain reaction
RNA synthesis
nonhuman
female
animal cell
article
priority journal
Drug Descriptors:
*growth differentiation factor 9
*transforming growth factor beta
luteinizing hormone receptor
messenger RNA
hyaluronic acid
urokinase receptor
cyclooxygenase 2
steroidogenic acute regulatory protein

RN (growth differentiation factor 9) 208778-50-1; (hyaluronic acid) 31799-91-4, 9004-61-9, 9067-32-7; (steroidogenic acute regulatory protein)
168183-61-7

L8 ANSWER 4 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 96247668 EMBASE
DN 1996247668
TI The gene encoding bone morphogenetic protein 8B is required for the initiation and maintenance of spermatogenesis in the mouse.
AU Zhao G.-Q.; Deng K.; Labosky P.A.; Liaw L.; Hogan B.L.M.
CS Department of Cell Biology, Howard Hughes Medical Institute, Vanderbilt University Medical School,Nashville, TN 37232-2175, United States
SO Genes and Development, (1996) 10/13 (1657-1669).
ISSN: 0890-9369 CODEN: GEDEEP
CY United States
DT Journal; Article
FS 021 Developmental Biology and Teratology
022 Human Genetics
LA English
SL English
AB Bone morphogenetic protein 8B (BMP8B) is a member of the **TGF**.
beta. superfamily of growth factors. In the mouse, Bmp8b is expressed in male germ cells of the testis and trophoblast cells of the placenta, suggesting that it has a role in spermatogenesis and **reproduction**. To investigate these possibilities, we have generated mice with a targeted mutation in Bmp8b. Here, we show that homozygous Bmp8b(tm1blh) mutant males exhibit variable degrees of germ-cell deficiency and **infertility**. Detailed analysis reveals two separable defects in the homozygous mutant testes. First, during early puberty (2 weeks old or younger) the germ cells of all homozygous mutants either fail to proliferate or show a marked reduction in proliferation and a delayed differentiation. Second, in adults, there is a significant increase in programmed cell death (apoptosis) of spermatocytes, leading to germ-cell depletion and sterility. Sertoli cells and Leydig cells appear relatively unaffected in mutants. This study therefore provides the first genetic evidence that a murine germ cell-produced factor, BMP8B, is required for the resumption of male germ-cell proliferation in early puberty, and for germ- cell survival and fertility in the adult.
CT Medical Descriptors:
*gene targeting
***male infertility: ET, etiology**
*male sterility: ET, etiology
*spermatogenesis
animal cell
animal experiment
animal tissue
article
cell death
controlled study
embryo
gene expression
germ cell
homozygosity
leydig cell
male
mouse
mouse mutant
newborn
nonhuman

postnatal development
priority journal
puberty
sertoli cell
testis development
trophoblast
Drug Descriptors:
*bone morphogenetic protein
transforming growth factor beta

L8 ANSWER 6 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 2000:213076 BIOSIS
DN PREV200000213076
TI Metabolic and ultrastructural abnormalities in semen from spinal cord injured men.
AU Monga, Manoj (1); Dunn, Kathleen (1); Rajasekaran, Mahadevan (1)
CS (1) San Diego, CA USA
SO Journal of Urology, (April, 2000) Vol. 163, No. 4 Suppl., pp. 297. Meeting Info.: 95th Annual Meeting of the American Urological Association, Inc. Atlanta, Georgia, USA April 29, 2000-May 04, 1999
ISSN: 0022-5347.
DT Conference
LA English
SL English
CC Reproductive System - General; Methods *16501
Biochemical Studies - General *10060
Nervous System - General; Methods *20501
Immunology and Immunochemistry - General; Methods *34502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
IT Major Concepts
Nervous System (Neural Coordination); Reproductive System (**Reproduction**)
IT Parts, Structures, & Systems of Organisms
semen: metabolic abnormalities, reproductive system, ultrastructural abnormalities
IT Diseases
asthenospermia: reproductive system disease/male; azoospermia: reproductive system disease/male; male **infertility**: reproductive system disease/male; necrospermia: reproductive system disease/male; spinal cord injury: injury, nervous system disease
IT Chemicals & Biochemicals
TGF-beta-1 [transforming growth factor-beta-1]
IT Alternate Indexing
Oligospermia (MeSH); **Infertility**, Male (MeSH); Spinal Cord Injuries (MeSH)
IT Methods & Equipment
ELISA: detection method; electron microscopy: microscopy method
IT Miscellaneous Descriptors
ejaculatory dysfunction; semen quality; Meeting Abstract; Meeting Poster
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): male, patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L8 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:298879 BIOSIS
DN PREV199900298879
TI Paracrine actions of growth differentiation factor-9 in the mammalian ovary.
AU Elvin, Julia A. (1); Clark, Amander T. (1); Wang, Pei (1); Wolfman, Neil M.; Matzuk, Martin M. (1)
CS (1) Department of Pathology, Baylor College of Medicine, Houston, TX, 77030 USA
SO Molecular Endocrinology, (June, 1999) Vol. 13, No. 6, pp. 1035-1048. ISSN: 0888-8809.
DT Article
LA English
SL English
AB Although the transforming growth factor-beta (**TGF-beta**) superfamily is the largest family of secreted growth factors, surprisingly few downstream target genes in their signaling pathways have been identified. Likewise, the identities of oocyte-derived secreted factors, which regulate important oocyte-somatic cell interactions, remain largely unknown. For example, oocytes are known to secrete paracrine growth factor(s) which are necessary for cumulus expansion, induction of hyaluronic acid synthesis, and suppression of LH receptor (LHR) mRNA synthesis. Our previous studies demonstrated that absence of the **TGF-beta** family member, growth differentiation factor-9 (GDF-9), blocks ovarian folliculogenesis at the primary follicle stage leading to **infertility**. In the present study, we demonstrate that mouse GDF-9 protein is expressed in all oocytes beginning at the type 3a follicle stage including antral follicles. To explore the biological functions of GDF-9 in the later stages of folliculogenesisand cumulus expansion, we produced mature, glycosylated, recombinant mouse GDF-9 using a Chinese hamster ovary cell expression system. A granulosa cell culture system was established to determine the role of GDF-9 in the regulation of several key ovarian gene products using semiquantitative RT-PCR. We find that recombinant GDF-9 induces hyaluronan synthase 2 (HAS2), cyclooxygenase 2 (COX-2), and steroidogenic acute regulator protein (StAR) mRNA synthesis but suppresses urokinase plasminogen activator (uPA) and LHR mRNA synthesis. Consistent with the induction of StAR mRNA by GDF-9, recombinant GDF-9 increases granulosa cell progesterone synthesis in the absence of FSH. Since induction of HAS2 and suppression of the protease uPA in cumulus cells are key events in the production of the hyaluronic acid-rich extracellular matrix which is produced during cumulus expansion, we determined whether GDF-9 could mimic this process. Using oocytectomized cumulus cell-oocyte complexes, we show thatrecombinant GDF-9 induces cumulus expansion in vitro. These studies demonstrate that GDF-9 can bind to receptors on granulosa cells to regulate the expression of a number of gene products. Thus, in addition to playing a critical function as a growth and differentiation factor during early folliculogenesis, GDF-9 functions as an oocyte-secreted paracrine factor to regulate several key granulosa cell enzymes involved in cumulus expansion and maintenance of an optimal oocyte microenvironment, processes which are essential for normal

L8 ANSWER 5 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 96201623 EMBASE
DN 1996201623
TI Changes in NK activities and **TGF-.beta.** concentration in the peritoneal cavity in endometriosis and their interaction related with **infertility**.
AU Mizumoto Y.
CS Department of Obstetrics/Gynecology, National Defence Medical College,Saitama, Japan
SO Acta Obstetrica et Gynaecologica Japonica, (1996) 48/6 (379-385). ISSN: 0300-9165 CODEN: AOGLAR
CY Japan
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
010 Obstetrics and Gynecology
026 Immunology, Serology and Transplantation
LA Japanese
SL English; Japanese
AB The purpose of this study was to clarify the relationship between NK activity and **TGF-.beta.** in the immune system in endometriosis. We investigated (1) the changes in the NK activity and concentration of **TGF-.beta.** in human peritoneal fluid (HPF), and (2) the effects of HPF and **TGF-.beta.** on the development of early mice embryos. In a rat model of experiment endometriosis, we observed the effects of tissue culture supernatants of peritoneum on NK activity in rat cells, and obtained the following results. (1) NK activity of peripheral lymphocytes in healthy women was significantly suppressed in the presence of HPF of endometriosis. (2) The concentrations of **TGF-.beta.** significantly higher in HPF of endometriosis than in HPF of healthy women. (3) Both HPF of endometriosis and **TGF-.beta.** significantly inhibited the development of early mice embryos. (4) The supernatants prepared from the intact peritoneum of the rat model showed marked inhibition of NK activity compared to control rats, although the peritoneum was obtained from a region distant from the implanted endometrium. These results suggest that ectopic endometrial tissues may cause a change in the cell-mediated immune system and subsequently exert an adverse effect on human **reproduction**.
CT Medical Descriptors:
*endometriosis: ET, etiology
female infertility: ET, etiology
*natural killer cell
animal cell
animal model
article
cellular immunity
controlled study
embryo
embryo development
female
human
human cell
mouse
nonhuman
peritoneal fluid
rat
spleen cell
Drug Descriptors:

*transforming growth factor beta: EC, endogenous compound

ovulation, fertilization, and female **reproduction**.
CC Reproductive System - Physiology and Biochemistry *16504
Cytology and Cytochemistry - Animal *02506
Endocrine System - Gonads and Placenta *17006
BC Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Endocrine System (Chemical Coordination and Homeostasis); Reproductive System (**Reproduction**)
IT Parts, Structures, & Systems of Organisms
oocyte: reproductive system; ovary: reproductive system
IT Chemicals & Biochemicals
growth differentiation factor-9
IT Miscellaneous Descriptors
fertilization; ovulation
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L8 ANSWER 8 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:359308 BIOSIS
DN PREV199799665711
TI Apoptosis in adult mouse testis induced by experimental cryptorchidism.
AU Ohta, Y. (1); Nishikawa, A.; Fukazawa, Y.; Urushitani, H.; Matsuzawa, A.; Nishina, Y.; Iguchi, T.
CS (1) Lab. Anim. Sci., Dep. Vet. Sci., Fac. Agric., Tottori Univ., Koyama, Tottori 680 Japan
SO Acta Anatomica, Vol. 157, No. 3, pp. 195-204.
ISSN: 0001-5180.
DT Article
LA English
AB Induction of cryptorchidism in the mouse causes **infertility** due to disruption of spermatogenesis including reduction of germ cells; however, the cellular mechanism responsible for the degenerative changes in cryptorchid testis is still unclear. In surgically induced bilateral cryptorchidism of 3-month-old C57BL/Tw mice, cellular changes in the cryptorchid testis were studied 1, 2, 3, 7, 14 and 21 days after the operation by electron microscopy, DNA fragmentation, in situ 3'-end labeling, serum and testicular testosterone measurements and gene expression. Although the testis showed DNA fragmentation even in intact mice, the cryptorchidism increased the degree of the fragmentation at 1 postcryptorchidism (p.c.) day. Apoptosis was encountered mainly in spermatids and spermatocytes. The number of apoptotic cells in the cryptorchid testis showed a 7-fold increase at 1 p.c. day as compared to the intact testis, then it gradually decreased. Serum testosterone levels showed a significant decrease at 2 p.c. days and remained low thereafter. Expression of transforming growth factor-beta-2 (**TGF-beta**-2), **TGF-beta**-3, tumor necrosis factor-alpha receptor and Fas mRNAs increased in the cryptorchid testis within 24 h after the operation. In lpr-cg and lpr mice lacking functional Fas, gld mice lacking functional Fas ligand and lpr-cg-gld mice lacking both functional Fas and Fas ligand, the experimental cryptorchidism also induced apoptosis in germ cells at 1 p.c. day. The present results indicate that cryptorchidism induces apoptotic dell death in germ cells, and that testosterone reduction and the Fas system may not be significantly involved in the apoptosis of male germ cells.
CC Cytology and Cytochemistry - Animal *02506
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Metabolism - Sterols and Steroids *13008
Metabolism - Proteins, Peptides and Amino Acids *13012
Reproductive System - Physiology and Biochemistry *16504
Endocrine System - General *17002
Endocrine System - Gonads and Placenta *17006
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Development; Endocrine System (Chemical Coordination and Homeostasis); Membranes (Cell Biology); Metabolism; Reproductive System (**Reproduction**)
IT Chemicals & Biochemicals
TESTOSTERONE
IT Miscellaneous Descriptors
ADULT; APOPTOSIS; CELL BIOLOGY; CONGENITAL DISEASE; CRYPTORCHIDISM; C57BL/TW; ENDOCRINE DISEASE/GONADS; FAS MESSENGER RNA; GERM CELLS;

INFERTILITY; REPRODUCTIVE SYSTEM; REPRODUCTIVE SYSTEM DISEASE; REPRODUCTIVE SYSTEM DISEASE/FEMALE; REPRODUCTIVE SYSTEM DISEASE/MALE; SERUM; SPERMATOGENESIS; TESTIS; TESTOSTERONE; TRANSFORMING GROWTH FACTOR-BETA-2; TUMOR NECROSIS FACTOR-ALPHA RECEPTOR

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

RN 58-22-0 (TESTOSTERONE)

L8 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:364490 BIOSIS
DN PREV199699086846
TI The gene encoding bone morphogenetic protein 8B is required for the initiation and maintenance of spermatogenesis in the mouse.
AU Zhao, Guang-Quan (1); Deng, Keyu; Labosky, Patricia A. (1); Liaw, Lucy; Hogan, Brigid L. M. (1)
CS (1) Howard Hughes Med. Inst., Vanderbilt Univ. Med. Sch., Nashville, TN 37232-2175 USA
SO Genes & Development, (1996) Vol. 10, No. 13, pp. 1657-1669. ISSN: 0890-9369.
DT Article
LA English
AB Bone morphogenetic protein 8B (BMP8B) is a member of the **TGF-beta** superfamily of growth factors. In the mouse, Bmp8b is expressed in male germ cells of the testis and trophoblast cells of the placenta, suggesting that it has a role in spermatogenesis and **reproduction**. To investigate these possibilities, we have generated mice with a targeted mutation in Bmp8b. Here, we show that homozygous Bmp8b-tm1blh mutant males exhibit variable degrees of germ-cell deficiency and **infertility**. Detailed analysis reveals two separable defects in the homozygous mutant testes. First, during early puberty (2 weeks old or younger) the germ cells of all homozygous mutants either fail to proliferate or show a marked reduction in proliferation and a delayed differentiation. Second, in adults, there is a significant increase in programmed cell death (apoptosis) of spermatocytes, leading to germ-cell depletion and sterility. Sertoli cells and Leydig cells appear relatively unaffected in mutants. This study therefore provides the first genetic evidence that a murine germ cell-produced factor, BMP8B, is required for the resumption of male germ-cell proliferation in early puberty, and for germ-cell survival and fertility in the adult.
CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules 10506
Pathology, General and Miscellaneous - Necrosis *12510
Reproductive System - Pathology *16506
Endocrine System - General *17002
Endocrine System - Gonads and Placenta *17006
Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
Developmental Biology - Embryology - General and Descriptive *25502
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Muridae *86375
IT Major Concepts
Cell Biology; Development; Endocrine System (Chemical Coordination and Homeostasis); Genetics; Pathology; Reproductive System (**Reproduction**); Skeletal System (Movement and Support)
IT Miscellaneous Descriptors
APOPTOSIS; GERM CELL DEPLETION; **INFERTILITY**; PLACENTA; TESTES; TRANSFORMING GROWTH FACTOR-BETA; TROPHOBLAST
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

L8 ANSWER 10 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:276132 BIOSIS
DN PREV199698832261
TI Transforming growth factor-beta-1 and b2 induce inhibin and activin beta-B-subunit messenger ribonucleic acid levels in cultured human granulosa-luteal cells.
AU Eramaa, Marja (1); Ritvos, Olli
CS (1) Dep. Bacteriology Immunology, P.O. Box 21, 00014 Univ. Helsinki, Helsinki Finland
SO Fertility and Sterility, (1996) Vol. 65, No. 5, pp. 954-960. ISSN: 0015-0282.
DT Article
LA English
AB Objective: To examine the effect of transforming growth factor-beta (**TGF-beta**) on inhibin and activin subunit messenger ribonucleic acids. Design: Human granulosa-luteal cell culture model. Setting: Granulosa cells were obtained from women undergoing an IVF program in a private IVF clinic. Patients: Regularly menstruating women undergoing oocyte retrieval for IVF because of either tubal obstruction or **infertility** of the spouse. Interventions: For each experiment, cells of two to four patients were pooled, enzymatically dispersed, separated from red blood cells by centrifugation through Ficoll-Paque and cultured in vitro in the presence of **TGF-beta**-1 or **TGF-beta**-2 and/or hCG whereafter cellular RNA was extracted for Northern or dot blot filter hybridization with inhibin alpha-, beta-A, and beta-B-subunit complementary DNA probes. Results: Both **TGF-beta**-1 and **TGF-beta**-2 induced the expression of a 4.8-kb inhibin and activin beta-B-subunit messenger (mRNA) transcript in a time- and dose-dependent manner but had no effect on alpha- or beta-A-subunit mRNA levels. Human chorionic gonadotropin alone did not affect beta-B-subunit mRNA levels, but when administered together with **TGF-beta**-s, it prevented the induction of beta-B-subunit mRNAs. Conclusions: Our results suggest that in human ovary, granulosa, or thecal cell-derived **TGF-beta**-1 or -beta-2 may eventually locally modulate in a paracrine or autocrine manner the relative expression levels of inhibin and activin subunits favoring the formation of the inhibin and activin dimers containing the beta-B-subunit. The effect of **TGF-beta** is clearly different from that of gonadotropins, which potently induce the alpha- and beta-A-subunit mRNAs, indicating that distinct components of the human ovarian inhibin and activin system are regulated differentially by endocrine and local factors.
CC Cytology and Cytochemistry - Human *02508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Reproductive System - Physiology and Biochemistry *16504
Endocrine System - General *17002
Endocrine System - Gonads and Placenta *17006
Tissue Culture, Apparatus, Methods and Media *32500
BC Hominidae *86215

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Reproductive System (**Reproduction**)

IT Chemicals & Biochemicals
INHIBIN

IT Miscellaneous Descriptors
ACTIVIN BETA-B SUBUNIT; HUMAN CHORIONIC GONADOTROPIN; INHIBIN BETA-B-SUBUNIT; MESSENGER RNA; OVARIAN CELL; THECAL CELL; TRANSFORMING GROWTH FACTOR-BETA 1; TRANSFORMING GROWTH FACTOR-BETA 2

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Hominidae (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN 57285-09-3 (INHIBIN)

L8 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1993:506245 BIOSIS
DN PREV199396130252
TI Immunohistochemical localizations of **TGF-beta** in the developing rat gonads.
AU Koike, Satoshi (1); Noumura, Tetsuo
CS (1) Upjohn Pharmaceutics Limited, Wadai, Tsukuba, Ibaraki 300-42 Japan
SO Zoological Science (Tokyo), (1993) Vol. 10, No. 4, pp. 671-677.
ISSN: 0289-0003.
DT Article
LA English
AB Beta types of transforming growth factor (**TGF-beta**-s) are known to have a variety of types of endocrine, paracrine and autocrine roles in the adult and embryonic tissues. In order to clarify the participation of **TGF-beta** in rat gonadal differentiation, immunohistochemical expression of **TGF-beta** was chronologically studied in perinatal rat gonads. Sprague-Dawley rat gonads from gestational day (GD) 13 to postnatal day (PD) 21 were fixed in Methacarn solution and stained with a polyclonal antibody against native porcine platelet **TGF-beta** in the rabbit by using avidin-biotin complex technique. Immunohistochemical reactivity to **TGF-beta** was positive in the germ cells of both sexes from GD 13 to PD 21. Moderate and marked staining was seen in male germ cells from GD 16 to PD 21 and in female germ cells from GD 21 to PD 11. Leydig/interstitial cells in male gonads were stained from GD 15, and moderate and marked staining from GD 16 to PD 11. On the other hand, the Sertoli or peritubular cells was not stained during the perinatal period. In contrast to the male gonads, the granulosa and interstitial cells in female gonads were stained on PDs 11 and 21. The Wolffian ducts in males and the Muellerian ducts in females expressed positive but weak reactivity during the perinatal period. The mesonephric tubules were faintly stained from GD 13 to 18. These results indicate that **TGF-beta** shows discrete cell-specific patterns of expression at various stages of the rat gonadal development and may participate in the rat gonadal development and differentiation.
CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Reproductive System - Physiology and Biochemistry *16504
Endocrine System - General *17002
Developmental Biology - Embryology - Morphogenesis, General *25508
Immunology and Immunochemistry - General; Methods *34502
BC Muridae *86375
IT Major Concepts
Cell Biology; Development; Endocrine System (Chemical Coordination and Homeostasis); Immune System (Chemical Coordination and Homeostasis); Reproductive System (**Reproduction**)
IT Miscellaneous Descriptors
LHRH; MALE **INFERTILITY**; PLASMA GONADOTROPIN; PROLACTIN; TESTOSTERONE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals;

rodents; vertebrates

L8 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2000 ACS
AN 1999:368419 CAPLUS
DN 131:125885
TI Paracrine actions of growth differentiation factor-9 in the mammalian ovary
AU Elvin, Julia A.; Clark, Amander T.; Wang, Pei; Wolfman, Neil M.; Matzuk, Martin M.
CS Department of Pathology, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, 77030, USA
SO Mol. Endocrinol. (1999), 13(6), 1035-1048
CODEN: MOENEN; ISSN: 0888-8809
PB Endocrine Society
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB Although the transforming growth factor-.beta. (**TGF**-. **beta**.) superfamily is the largest family of secreted growth factors, surprisingly few downstream target genes in their signaling pathways have been identified. Likewise, the identities of oocyte-derived secreted factors, which regulate important oocyte-somatic cell interactions, remain largely unknown. For example, oocytes are known to secrete paracrine growth factor(s) which are necessary for cumulus expansion, induction of hyaluronic acid synthesis, and suppression of LH receptor (LHR) mRNA synthesis. The authors' previous studies demonstrated that absence of the **TGF**-.**beta**. family member, growth differentiation factor-9 (GDF-9), blocks ovarian folliculogenesis at the primary follicle stage leading to **infertility**. In the present study, the authors demonstrate that mouse GDF-9 protein is expressed in all oocytes beginning at the type 3a follicle stage including antral follicles. To explore the biol. functions of GDF-9 in the later stages of folliculogenesis and cumulus expansion, the authors produced mature, glycosylated, recombinant mouse GDF-9 using a Chinese hamster ovary cell expression system. A granulosa cell culture system was established to det. the role of GDF-9 in the regulation of several key ovarian gene products using semiquant. RT-PCR. The authors found that recombinant GDF-9 induces hyaluronan synthase 2 (HAS2), cyclooxygenase 2 (COX-2), and steroidogenic acute regulator protein (StAR) mRNA synthesis but suppresses urokinase plasminogen activator (uPA) and LHR mRNA synthesis. Consistent with the induction of StAR mRNA by GDF-9, recombinant GDF-9 increases granulosa cell progesterone synthesis in the absence of FSH. Since induction of HAS2 and suppression of the protease uPA in cumulus cells are key events in the prodn. of the hyaluronic acid-rich extracellular matrix which is produced during cumulus expansion, the authors detd. whether GDF-9 could mimic this process. Using oocytectomized cumulus cell-oocyte complexes, the authors show that recombinant GDF-9 induces cumulus expansion in vitro. These studies demonstrate that GDF-9 can bind to receptors on granulosa cells to regulate the expression of a no. of gene products. Thus, in addn. to playing a crit. function as a growth and differentiation factor during early folliculogenesis, GDF-9 functions as an oocyte-secreted paracrine factor to regulate several key granulosa cell enzymes involved in cumulus expansion and maintenance of an optimal oocyte

microenvironment, processes which are essential for normal ovulation, fertilization, and female **reprodn**.
ST growth differentiation factor 9 ovary folliculogenesis; cumulus expansion growth differentiation factor 9
IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(StAR (steroidogenic acute regulatory); growth differentiation factor-9
paracrine actions in mammalian ovary)
IT Ovary
(cumulus; growth differentiation factor-9 paracrine actions in mammalian ovary)
IT Ovary
(follicle cell; growth differentiation factor-9 paracrine actions in mammalian ovary)
IT Oogenesis
Ovary
(growth differentiation factor-9 paracrine actions in mammalian ovary)
IT Gonadotropin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(growth differentiation factor-9 paracrine actions in mammalian ovary)
IT Egg
(oocyte; growth differentiation factor-9 paracrine actions in mammalian
ovary)
IT 39346-43-5, Hyaluronan synthase 39391-18-9
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(2; growth differentiation factor-9 paracrine actions in mammalian ovary)
IT 208778-50-1, Growth differentiation factor-9
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BIOL (Biological study); PROC (Process)
(growth differentiation factor-9 paracrine actions in mammalian ovary)
IT 57-83-0, Progesterone, biological studies 139639-24-0, Urokinase plasminogen activator
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(growth differentiation factor-9 paracrine actions in mammalian ovary)
RE.CNT 48
RE
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L8 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2000 ACS
AN 1996:424726 CAPLUS
DN 125:78439
TI The gene encoding bone morphogenetic protein 8B is required for the initiation and maintenance of spermatogenesis in the mouse
AU Zhao, Guang-Quan; Deng, Keyu; Labosky, Patricia A.; Liaw, Lucy; Hogan, Brigid L. M.
CS Howard Hughes Medical Institute, Vanderbilt University Medical School, Nashville, TN, 37232-2175, USA
SO Genes Dev. (1996), 10(13), 1657-1669
CODEN: GEDEEP; ISSN: 0890-9369
DT Journal
LA English
CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 13
AB Bone morphogenetic protein 8B (BMP8B) is a member of the **TGF**. **beta**. superfamily of growth factors. In the mouse, Bmp8b is expressed in male germ cells of the testis and trophoblast cells of the placenta, suggesting that is has a role in spermatogenesis and **reprodn**. To investigate these possibilities, we have generated mice with a targeted mutation in Bmp8b. Here, we show that homozygous Bmp8btm1bh mutant males exhibit variable degrees of germ-cell deficiency and **infertility**. Detailed anal. reveals two separable defects in the homozygous mutant testes. First, during early puberty (2 wk old or younger) the germ cells of all homozygous mutants either fail to proliferate or show a marked redn. in proliferation and a delayed differentiation. Second, in adults, there is a significant increase in programmed cell death (apoptosis) of spermatocytes, leading to germ-cell depletion and sterility. This study therefore provides the first genetic evidence that a murine germ cell-produced factor, BMP8B, is required for the resumption of male-germ proliferation in early puberty, and for germ-cell survival and fertility in the adult.
ST bone morphogenetic protein 8B mouse spermatogenesis
IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Bmp8b; the gene encoding bone morphogenetic protein 8B is required for the initiation and maintenance of spermatogenesis in the mouse)
IT Mouse
Spermatogenesis
(the gene encoding bone morphogenetic protein 8B is required for the initiation and maintenance of spermatogenesis in the mouse)
IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(bone morphogenetic proteins, 8B; the gene encoding bone morphogenetic protein 8B is required for the initiation and maintenance of spermatogenesis in the mouse)

L8 ANSWER 14 OF 17 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1999:438072 SCISEARCH
GA The Genuine Article (R) Number: 202UE
TI Paracrine actions of growth differentiation factor-9 in the mammalian ovary
AU Elvin J A; Clark A T; Wang P; Wolfman N M; Matzuk M M (Reprint)
CS BAYLOR COLL MED, DEPT PATHOL, 1 BAYLOR PLAZA, HOUSTON, TX 77030 (Reprint);
BAYLOR COLL MED, DEPT PATHOL, HOUSTON, TX 77030; BAYLOR COLL MED, DEPT MOL
& HUMAN GENET, HOUSTON, TX 77030; BAYLOR COLL MED, DEPT CELL BIOL, HOUSTON, TX 77030; GENET INST INC, CAMBRIDGE, MA 02140
CYA USA
SO MOLECULAR ENDOCRINOLOGY, (JUN 1999) Vol. 13, No. 6, pp. 1035-1048.
Publisher: ENDOCRINE SOC, 4350 EAST WEST HIGHWAY SUITE 500, BETHESDA, MD 20814-4110.
ISSN: 0888-8809.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 48
AB Although the transforming growth factor-beta (**TGF-beta**) superfamily is the largest family of secreted growth factors, surprisingly few downstream target genes in their signaling pathways have been identified. Likewise, the identities of oocyte-derived secreted factors, which regulate important oocyte-somatic cell interactions, remain largely unknown. For example, oocytes are known to secrete paracrine growth factor(s) which are necessary for cumulus expansion, induction of hyaluronic acid synthesis, and suppression of LH receptor (LHR) mRNA synthesis. Our previous studies demonstrated that absence of the **TGF-beta** family member, growth differentiation factor-9 (GDF-9), blocks ovarian folliculogenesis at the primary follicle stage leading to **infertility**. In the present study, we demonstrate that mouse GDF-9 protein is expressed in all oocytes beginning at the type 3a follicle stage including antral follicles. To explore the biological functions of GDF-9 in the later stages of folliculogenesis and cumulus expansion, we produced mature, glycosylated, recombinant mouse GDF-9 using a Chinese hamster ovary cell expression system. A granulosa cell culture system was established to determine the role of GDF-9 in the regulation of several key ovarian gene products using semiquantitative RT-PCR. We find that recombinant GDF-9 induces hyaluronan synthase 2 (HAS2), cyclooxygenase 2 (COX-2), and steroidogenic acute regulator protein (StAR) mRNA synthesis but suppresses urokinase plasminogen activator (uPA) and LHR mRNA synthesis. Consistent with the induction of StAR mRNA by GDF-9, recombinant GDF-9 increases granulosa cell progesterone synthesis in the absence of FSH. Since induction of HASP and suppression of the protease uPA in cumulus cells are key events in the production of the hyaluronic acid-rich extracellular matrix which is produced during cumulus expansion, we determined whether GDF-9 could mimic this process. Using oocytectomized cumulus cell-oocyte complexes, we show that recombinant GDF-9 induces cumulus expansion in vitro. These studies demonstrate that GDF-9 can bind to receptors on granulosa cells to

regulate the expression of a number of gene products. Thus, in addition to playing a critical function as a growth and differentiation factor during early folliculogenesis, GDF-9 functions as an oocyte-secreted paracrine factor to regulate several key granulosa cell enzymes involved in cumulus expansion and maintenance of an optimal oocyte microenvironment, processes which are essential for normal ovulation, fertilization, and female **reproduction**.

CC ENDOCRINOLOGY & METABOLISM

STP KeyWords Plus (R): LUTEINIZING-HORMONE RECEPTOR; FOLLICLE-STIMULATING-HORMONE; MESSENGER-RIBONUCLEIC-ACID; ACUTE REGULATORY PROTEIN; GRANULOSA-CELLS; MOUSE OOCYTES; FACTOR-BETA; HYALURONIC-ACID; CUMULUS CELLS; ACTIVIN RECEPTOR

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
ARAKANE F	1997	272	32656	J BIOL CHEM
BUCCIONE R	1990	138	16	DEV BIOL
CANIPARI R	1995	167	371	DEV BIOL
CARABATSOS M	1998	203	373	DEV BIOL
CLARK B J	1995	9	1346	MOL ENDOCRINOL
DONG J W	1996	383	531	NATURE
DRAPER L	1998			80 ANN M END SOC NEW
DRAPER L B	1998	273	398	J BIOL CHEM
DUBE J L	1998	12	1809	MOL ENDOCRINOL
ELFOULY M A	1970	87	288	ENDOCRINOLOGY
ELVIN J A	1999	13	1018	MOL ENDOCRINOL
ELVIN J A	1998	3	183	REV REPROD
EPPIG J J	1997	56	976	BIOL REPROD
EPPIG J J	1997	12	127	HUM REPROD
EPPIG J J	1993	34	450	MOL REPROD DEV
EPPIG J J	1998	49	327	MOL REPROD DEV
EPPIG J J	1994	5	51	SEMIN DEV BIOL
FULOP C	1997	337	261	ARCH BIOCHEM BIOPHYS
HELDIN C H	1997	390	465	NATURE
INCERTI B	1994	1222	125	BBA-MOL CELL RES
LAU A L	1999			IN PRESS GRAVITATION
LAWRENCE T S	1980	106	1114	ENDOCRINOLOGY
LIM H	1997	91	197	CELL
LYONS K	1989	86	4554	P NATL ACAD SCI USA
LYONS K M	1989	3	1657	GENE DEV
MAHMOUDI M	1989	7	331	BIOTECHNIQUES
MASSAGUE J	1997	7	187	TRENDS CELL BIOL
MATZUK M M	1995	374	356	NATURE
MCGRATH S A	1995	9	131	MOL ENDOCRINOL
MCPHERRON A C	1993	268	3444	J BIOL CHEM
MEDURI G	1992	131	366	ENDOCRINOLOGY
NEKOLA M V	1971	4	154	BIOL REPROD
NISHIMORI K	1996	1	203	REV REPROD
RENNERT H	1993		147	OVARY
RICHARDS J S	1988	50	441	ANN REV PHYSL
SALUSTRI A	1990	138	26	DEV BIOL
SALUSTRI A	1989	264	13840	J BIOL CHEM
SALUSTRI A	1990	265	19517	J BIOL CHEM
SALUSTRI A	1996	4	313	ZYGOTE
SAMBROOK J	1989			MOL CLONING LAB MANU

SCHUETZ A W	1981	108	457	ENDOCRINOLOGY
SIDIS Y	1998	59	807	BIOL REPROD
SKINNER M K	1987	121	786	ENDOCRINOLOGY
SPICER A P	1996	271	23400	J BIOL CHEM
STERNECK E	1997	11	2153	GENE DEV
TIRONE E	1997	272	4787	J BIOL CHEM
VANDERHYDEN B C	1993	133	423	ENDOCRINOLOGY
WASSARMAN P M	1994		79	PHYSIOL REPRODUCTION

L8 ANSWER 15 OF 17 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1998:514160 SCISEARCH
GA The Genuine Article (R) Number: ZX102
TI Transforming growth factor-beta(1), insulin-like growth factors, and insulin-like growth factor binding proteins in ovarian follicular fluid are differentially regulated by the type of ovarian hyperstimulation used for in vitro fertilization
AU Fried G (Reprint); Wramsby H; Tally M
CS KAROLINSKA HOSP, DEPT WOMAN & CHILD HLTH, REPROD MED CTR, DIV OBSTET & GYNECOL, S-17176 STOCKHOLM, SWEDEN (Reprint); KAROLINSKA HOSP, DEPT MOL MED, UNIT ENDOCRINOL & DIABET, S-17176 STOCKHOLM, SWEDEN
CYA SWEDEN
SO FERTILITY AND STERILITY, (JUL 1998) Vol. 70, No. 1, pp. 129-134. Publisher: AMER SOC REPRODUCTIVE MEDICINE, 1209 MONTGOMERY HIGHWAY, BIRMINGHAM, AL 35216-2809.
ISSN: 0015-0282.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 27
AB Objective: To determine the effects of hMG and highly purified FSH on follicular production of the ovarian growth factors transforming growth factor-beta(1) (**TGF-beta**(1)), insulin-like growth factors I and II (IGF-I and IGF-II), and insulin-like growth factor binding proteins-1 and -3 (IGFBP-1 and IGFBP-3).
Design: Controlled clinical study.
Setting: University IVF program.
Patient(s): One hundred twenty women who were <38 years old and had a >3-year duration of **infertility** in their present relationship participated in the study.
Intervention(s): Follicular fluid and matched serum were collected at oocyte pick-up and analyzed for growth factors and E-2 with the use of ELISA and RIA.
Main Outcome Measure(s): Levels of **TGF-beta**(1), IGF-I, IGF-II, IGFBP-1, and IGFBP-3 in follicular fluid and levels of E-2 in serum were measured.
Result(s): Compared with highly purified FSH, ovarian hyperstimulation with hMG produced lower levels of **TGF-beta**(1) and IGF-I and higher levels of IGFBP-1. Levels of IGF-II and IGFBP-3 were similar with the 2 treatments.
Conclusion(s): In patients undergoing IVF, the follicular expression of **TGF-beta**(1), IGF-I, and IGFBP-1 was regulated differently by highly purified FSH compared with a preparation containing FSH and LH in a 1:1 ratio (hMG). The results indicate that FSH and LH control ovarian production of these growth factors differentially.
(Fertil Steril(R) 1998;70:129-34 (C) 1998 by American Society for Reproductive Medicine.).
CC OBSTETRICS & GYNECOLOGY
ST Author Keywords: gonadotropins; assisted **reproduction**; **TGF-beta**; IGF; ovary
STP KeyWords Plus (R): THECA-INTERSTITIAL CELLS; FACTOR-BETA; **TGF-BETA**; LUTEINIZING-HORMONE; FACTOR-I; HAMSTER OVARY; EXPRESSION; RECEPTOR; ESTRADIOL-17-BETA; LOCALIZATION
RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)

ADASHI E Y	1991	6	1213	HUM REPROD
ANDERSON E	1993	25	49	TISSUE CELL
DORRINGTON J H	1993	44	441	J STEROID BIOCHEM
FOURNET N	1996	137	166	ENDOCRINOLOGY
FRIED G	1996	11	101	HUM REPROD
GIUDICE L C	1992	13	641	ENDOCR REV
HALVORSON L M	1996	65	459	FERTIL STERIL
HERNANDEZ E R	1990	127	2804	ENDOCRINOLOGY
IMBENOTTE J	1992	199	229	EXP CELL RES
LIN H Y	1993	3	14	TRENDS CELL BIOL
LOPEZCASILLAS F	1993	73	1435	CELL
MAGOFFIN D A	1994	51	766	BIOL REPROD
MAGOFFIN D A	1995	53	627	BIOL REPROD
MARTIN J L	1991	128	1425	ENDOCRINOLOGY
MASON H D	1996	81	276	J CLIN ENDOCR METAB
MASSAGUE J	1992	12	81	CANCER SURV
MAU Y H L	1996		16	6 OV WORKSH OV CELL
MULHERON G W	1992	74	458	J CLIN ENDOCR METAB
POVOA G	1984	107	563	ACTA ENDOCRINOL-COP
ROSENFELD R G	1990	46	99	RECENT PROG HORM RES
ROY S K	1992	46	595	BIOL REPROD
ROY S K	1995	136	4610	ENDOCRINOLOGY
SPORN M B	1992	119	1017	J CELL BIOL
TAIPALE J	1994	124	171	J CELL BIOL
TALLY M	1994	79	1576	J CLIN ENDOCR METAB
TAYMOR M L	1996	65	235	FERTIL STERIL
VEIT C R	1988	122	1227	ENDOCRINOLOGY

L8 ANSWER 16 OF 17 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1998:298963 SCISEARCH
GA The Genuine Article (R) Number: ZG375
TI Regulation of cellular and system function by activin
AU Woodruff T K (Reprint)
CS NORTHWESTERN UNIV, CTR ENDOCRINOL METAB & MOL MED, DEPT MED, DIV ENDOCRINOL METAB & MOL MED, CHICAGO, IL 60611 (Reprint)
CYA USA
SO BIOCHEMICAL PHARMACOLOGY, (1 APR 1998) Vol. 55, No. 7, pp. 953-963. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB. ISSN: 0006-2952.
DT General Review; Journal
FS LIFE
LA English
REC Reference Count: 155
AB Activin is an important molecule that regulates hormonogenesis, cellular homeostasis (divide or die pathways), and differentiation programs (developmentally and in adult cells). The cellular mechanisms that integrate an activin signal into a physiological response include a binary receptor complex and tandem serine threonine kinases, intracellular signal mediators, and nuclear transcription factors. Activin antagonists (inhibins) and bioneutralizing binding proteins (follistatins) act as gating molecules to ensure accurate delivery of activin signals to cellular machinery. Correct execution of an activin cue intracellularly permits actions as fundamental as embryonic mesoderm development, neuronal survival, hematopoietic function, and reproductive cyclicity. Absent or incorrect activin signaling results in phenotypes as catastrophic as embryonic lethality, tumor formation, and **infertility**. The general ways in which a cell senses and responds to an activin signal will be reviewed in the first part of this paper. The role of this ligand in reproductive function will also be examined as a specific example of activin activity. (C) 1998 Elsevier Science Inc.
CC PHARMACOLOGY & PHARMACY; BIOCHEMISTRY & MOLECULAR BIOLOGY
ST Author Keywords: **reproduction**; development; ovary; activin; inhibin; TGF
STP KeyWords Plus (R): TRANSFORMING GROWTH-FACTOR; FOLLICLE-STIMULATING-HORMONE; HUMAN MENSTRUAL-CYCLE; MESSENGER RIBONUCLEIC-ACIDS; **TGF -BETA** RECEPTOR; SERINE THREONINE KINASE; GONADOTROPIN-RELEASING-HORMONE; PROTEIN TRANSFERASE-ALPHA; TRANSGENIC MOUSE MODELS; TUMOR-SUPPRESSOR GENES
RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
ANAWALT B D	1996	81	3341	J CLIN ENDOCR METAB
ATTISANO L	1992	86	97	CELL
ATTISANO L	1993	75	671	CELL
ATTISANO L	1996	16	1066	MOL CELL BIOL
BESECKE L M	1996	137	3667	ENDOCRINOLOGY
BRANNIAN J D	1992	75	756	J CLIN ENDOCR METAB
BRAWTAL R	1994	13	253	J MOL ENDOCRINOL
CAMERON A M	1995	83	463	CELL
CAMERON V A	1994	134	799	ENDOCRINOLOGY
CHEN F	1995	92	1565	P NATL ACAD SCI USA

CHEN R H	1995	270	12235	J BIOL CHEM
CHEN R H	1995	377	548	NATURE
CHEN X	1996	383	691	NATURE
CORRIGAN A Z	1991	128	1682	ENDOCRINOLOGY
DAOPIN S	1993	17	176	PROTEIN-STRUCT FUNCT
DEPAOLO L V	1991	128	668	ENDOCRINOLOGY
DEPAOLO L V	1991	198	500	P SOC EXP BIOL MED
DERYNCK R	1996	87	173	CELL
DEWINTER J P	1996	224	323	EXP CELL RES
DONG J	1996	383	531	NATURE
DURBEC P	1996	381	789	NATURE
EBNER R	1993	262	900	SCIENCE
EPPERT K	1996	86	543	CELL
ESTEVEZ M	1993	365	644	NATURE
FANG J M	1996	228	669	BIOCHEM BIOPH RES CO
FINDLAY J K	1993	48	15	BIOL REPROD
FRANZEN P	1995	207	682	BIOCHEM BIOPH RES CO
FRANZEN P	1993	75	681	CELL
FRASER H M	1993	4	187	TRENDS ENDOCRIN MET
GRAFF J M	1996	85	479	CELL
GRIEDER N C	1995	81	791	CELL
GRIFFITH D L	1996	93	878	P NATL ACAD SCI USA
GROOME N P	1996	81	1401	J CLIN ENDOCR METAB
HAHN S A	1996	271	350	SCIENCE
HANCOCK J F	1989	57	1167	CELL
HARADA K	1996	81	2125	J CLIN ENDOCR METAB
HARTSOUGH M T	1996	271	22368	J BIOL CHEM
HASHIMOTO M	1993	133	1934	ENDOCRINOLOGY
HE W W	1993	196	133	DEV DYNAM
HILLIER S G	1993	687	29	ANN NY ACAD SCI
HILLIER S G	1991	72	1206	J CLIN ENDOCR METAB
HILLIER S G	1994		1	MOL BIOL FEMALE REPR
HILLIER S G	1991	75	R1	MOL CELL ENDOCRINOL
HIROBE S	1994	50	1238	BIOL REPROD
HOGAN B L M	1996	10	1580	GENE DEV
HOODLESS P A	1996	85	489	CELL
ILLINGWORTH P J	1996	81	1321	J CLIN ENDOCR METAB
ILLINGWORTH P J	1996	81	1471	J CLIN ENDOCR METAB
IOZZO R V	1997	272	5219	J BIOL CHEM
JAATINEN R	1996	81	3877	J CLIN ENDOCR METAB
JAYARAMAN T	1992	267	9474	J BIOL CHEM
KALKHOVEN E	1995	6	1151	CELL GROWTH DIFFER
KAWABATA M	1995	270	29628	J BIOL CHEM
KINGSLEY D M	1994	8	133	GENE DEV
KLEIN N A	1996	81	2742	J CLIN ENDOCR METAB
KRUMMEN L A	1994	50	734	BIOL REPROD
KRUMMEN L A	1993	132	431	ENDOCRINOLOGY
KUMAR T R	1995	238	233	J INTERN MED
LABONNE C	1994	120	463	DEVELOPMENT
LAGNA G	1996	383	832	NATURE
LEBRUN J J	1997	17	1682	MOL CELL BIOL
LI R H	1995	136	849	ENDOCRINOLOGY
LI W	1992	75	285	J CLIN ENDOCR METAB
LIN H Y	1992	68	775	CELL
LIU F	1996	381	620	NATURE
LOCKWOOD G M	1996	45	741	CLIN ENDOCRINOL
MACIASSILVA M	1996	87	1215	CELL
MACNICOL A M	1993	73	571	CELL

MASSAGUE J	1992	12	81	CANCER SURV
MASSAGUE J	1996	27	41	CANCER SURV
MASSAGUE J	1996	85	947	CELL
MATHEWS L S	1991	65	973	CELL
MATHEWS L S	1994	15	310	ENDOCR REV
MATHEWS L S	1993	268	19013	J BIOL CHEM
MATZUK M M	1995	374	354	NATURE
MATZUK M M	1995	374	356	NATURE
MATZUK M M	1995	374	360	NATURE
MATZUK M M	1996	51	123	RECENT PROG HORM RES
MATZUK M M	1994	5	37	SEMIN CANCER BIOL
MAYO K E	1994	5	407	TRENDS ENDOCRIN MET
MCLACHLAN R I	1989	125	2787	ENDOCRINOLOGY
MCLACHLAN R I	1987	48	1001	FERTIL STERIL
MCPHERRON A C	1993	268	3444	J BIOL CHEM
MINE T	1992	186	205	BIOCHEM BIOPH RES CO
MIRO F	1996	137	464	ENDOCRINOLOGY
MIRO F	1992	75	1556	J CLIN ENDOCR METAB
MISHINA Y	1996	10	2577	GENE DEV
MOGAMI H	1995	136	2960	ENDOCRINOLOGY
MOLSKNESS T A	1996	81	4002	J CLIN ENDOCR METAB
MUTTUKRISHNA S	1994	9	1634	HUM REPROD
MUTTUKRISHNA S	1996	81	3328	J CLIN ENDOCR METAB
ODA S	1995	210	581	BIOCHEM BIOPH RES CO
OTSUKA M	1995	38	3264	J MED CHEM
PETRAGLIA F	1993	1	323	ENDOCR J
PETRAGLIA F	1995	80	558	J CLIN ENDOCR METAB
PETRAGLIA F	1994	84	278	OBSTET GYNECOL
PIRCHER R	1986	136	30	BIOCHEM BIOPH RES CO
QIAN S W	1994	33	12298	BIOCHEMISTRY-US
QIAN S W	1996	271	30656	J BIOL CHEM
RABINOVICI J	1992	89	1528	J CLIN INVEST
RAFTERY L A	1995	139	241	GENETICS
REDDI K	1990	33	547	CLIN ENDOCRINOL
RIGGINS G J	1996	13	347	NAT GENET
RIVIER C	1989	125	152	ENDOCRINOLOGY
RIVIER C	1991	129	2463	ENDOCRINOLOGY
ROBERTS A B	1990		419	PEPTIDE GROWTH FACTO
ROBERTS V J	1994	134	914	ENDOCRINOLOGY
ROBERTS V J	1996	137	4201	ENDOCRINOLOGY
ROBERTS V J	1993	77	1402	J CLIN ENDOCR METAB
ROBERTS V J	1994	79	1434	J CLIN ENDOCR METAB
ROBERTS V J	1996	364	473	J COMP NEUROL
ROSEFF S J	1989	69	1033	J CLIN ENDOCR METAB
ROY S K	1994	51	821	BIOL REPROD
SCHMITT J	1996	32	358	GENOMICS
SCHUTTE M	1996	56	2527	CANCER RES
SCHWALL R	1989	125	1420	ENDOCRINOLOGY
SCHWALL R H	1990	4	75	MOL ENDOCRINOL
SEKELSKY J J	1995	139	1347	GENETICS
STAEHLING K	1995	121	3393	DEVELOPMENT
STOUFFER R L	1994	50	888	BIOL REPROD
STOUFFER R L	1993	77	241	J CLIN ENDOCR METAB
SUN P D	1995	24	269	ANNU REV BIOPHYS BIO
TEIXEIRA J	1996	17	336	J ANDROL
TENDIJKE P	1994	269	16985	J BIOL CHEM
TENDIJKE P	1993	8	2879	ONCOGENE
TENDIJKE P	1994	264	101	SCIENCE

TREANOR J J S	1996	382	80	NATURE
TSUCHIDA K	1995	136	5493	ENDOCRINOLOGY
VALE W	1988	44	1	RECENT PROG HORM RES
VASSALLI A	1994	8	414	GENE DEV
VAUGHAN J M	1993	132	2038	ENDOCRINOLOGY
VENTURA F	1994	13	5581	EMBO J
VENTURA F	1996	271	13931	J BIOL CHEM
VERSCHUEREN K	1995	52	109	MECH DEVELOP
WALLACE E M	1996	44	17	CLIN ENDOCRINOL
WALLACE E M	1997	82	218	J CLIN ENDOCR METAB
WALLACE E M	1997	152	109	J ENDOCRINOL
WANG T	1996	86	435	CELL
WANG T W	1994	265	674	SCIENCE
WANG T W	1996	271	1120	SCIENCE
WANG X F	1991	67	797	CELL
WEISS J	1992	131	1403	ENDOCRINOLOGY
WIESER R	1995	14	2199	EMBO J
WILLIS S A	1996	10	367	MOL ENDOCRINOL
WOODRUFF T	1995	57	219	ANN REV PHYSL
WOODRUFF T K	1990	127	3196	ENDOCRINOLOGY
WOODRUFF T K	1993	132	2332	ENDOCRINOLOGY
WOODRUFF T K	1993	133	2998	ENDOCRINOLOGY
WOODRUFF T K	1996	137	5463	ENDOCRINOLOGY
WRANA J L	1994	14	944	MOL CELL BIOL
WRANA J L	1994	370	341	NATURE
WU R Y	1997	17	2521	MOL CELL BIOL
YAMASHITA H	1994	269	20172	J BIOL CHEM
YAMASHITA H	1995	130	217	J CELL BIOL
YINGLING J M	1996	93	8940	P NATL ACAD SCI USA

L8 ANSWER 17 OF 17 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 96:540916 SCISEARCH
GA The Genuine Article (R) Number: UX663
TI THE GENE ENCODING BONE MORPHOGENETIC PROTEIN 8B IS REQUIRED FOR THE INITIATION AND MAINTENANCE OF SPERMATOGENESIS IN THE MOUSE
AU ZHAO G Q; DENG K; LABOSKY P A; LIAW L; HOGAN B L M (Reprint)
CS VANDERBILT UNIV, SCH MED, HOWARD HUGHES MED INST, NASHVILLE, TN, 37232 (Reprint); VANDERBILT UNIV, SCH MED, HOWARD HUGHES MED INST, NASHVILLE, TN, 37232; VANDERBILT UNIV, SCH MED, DEPT CELL BIOL, NASHVILLE, TN, 37232
CYA USA
SO GENES & DEVELOPMENT, (01 JUL 1996) Vol. 10, No. 13, pp. 1657-1669. ISSN: 0890-9369.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 60
AB Bone morphogenetic protein 8B (BMPBB) is a member of the **TGF beta** superfamily of growth factors. In the mouse, Bmp8b is expressed in male germ cells of the testis and trophoblast cells of the placenta, suggesting that it has a role in spermatogenesis and **reproduction**. To investigate these possibilities, we have generated mice with a targeted mutation in Bmp8b. Here, we show that homozygous Bmp8b(tm1blh) mutant males exhibit variable degrees of germ-cell deficiency and **infertility**. Detailed analysis reveals two separable defects in the homozygous mutant testes. First, during early puberty (2 weeks old or younger) the germ cells of all homozygous mutants either fail to proliferate or show a marked reduction in proliferation and a delayed differentiation. Second, in adults, there is a significant increase in programmed cell death (apoptosis) of spermatocytes, leading to germ-cell depletion and sterility. Sertoli cells and Leydig cells appear relatively unaffected in mutants. This study therefore provides the first genetic evidence that a murine germ cell-produced factor, BMP8B, is required for the resumption of male germ-cell proliferation in early puberty, and for germ-cell survival and fertility in the adult.
CC DEVELOPMENTAL BIOLOGY; GENETICS & HEREDITY
ST Author Keywords: BMP8B; TARGETED GENE INACTIVATION; MALE GERM CELL; SPERMATOGENESIS; TESTIS DEGENERATION; FERTILITY
STP KeyWords Plus (R): RAT SEMINIFEROUS EPITHELIUM; SPERMATOGONIAL DEPLETION JSD; GROWTH-FACTOR; PATTERN-FORMATION; BETA SUPERFAMILY; SERTOLI CELLS; EXPRESSION; MICE; IDENTIFICATION; RECEPTOR
RF 94-3837 002; BONE MORPHOGENETIC PROTEINS; MURINE MESENCHYMAL PROGENITOR C3H10T1/2 CELLS INDUCES DIFFERENTIATION; RECOMBINANT BOMBYX-MORI NUCLEAR POLYHEDROSIS-VIRUS
94-1480 001; MYOGENIC HELIX-LOOP-HELIX TRANSCRIPTION FACTOR MYOD; BASIC REGION LEUCINE-ZIPPER; DNA-BINDING DOMAINS; MUSCLE DIFFERENTIATION; ID GENE INDUCTION
94-5801 001; MESANGIAL CELL APOPTOSIS; DNA STRAND BREAKS; APOPTOTIC MECHANISM
RE

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	113.94	114.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.34	-3.34

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